Interactive CardioVascular and Thoracic Surgery (2021) 1–5
doi:10.1093/icvts/ivaa326

ORIGINAL ARTICLE

Cite this article as: Schmiady MO, Hofmann M, Sromicki J, Halbe M, van Tilburg K, Aser R *et al.* Initiation of an inter-hospital extracorporeal membrane oxygenation transfer programme for critically ill patients with coronavirus disease 2019: bringing extracorporeal membrane oxygenation support to peripheral hospitals. Interact CardioVasc Thorac Surg 2021; doi:10.1093/icvts/ivaa326.

Initiation of an inter-hospital extracorporeal membrane oxygenation transfer programme for critically ill patients with coronavirus disease 2019: bringing extracorporeal membrane oxygenation support to peripheral hospitals

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Received 2 September 2020; received in revised form 31 October 2020; accepted 9 November 2020

Key question

How to establish an out-of-center ECMO program for critically ill COVID-19 patients?

Key findings

Proper patient selection and good preparation/ selection of the required material is essential.

Take-home message

Out-of-center ECMO implantation in well selected COVID-19 patients is feasible and safe if a well-established organization is available.

Abstract

OBJECTIVES: Extracorporeal membrane oxygenation (ECMO) is a resource-intensive, highly specialized and expensive therapy that is often reserved for high-volume centres. In recent years, we established an inter-hospital ECMO transfer programme that enables ECMO implants in peripheral hospitals. During the pandemic, the programme was expanded to include ECMO support in selected critically ill patients with coronavirus disease 2019 (COVID-19).

METHODS: This retrospective single-centre study reports the technical details and challenges encountered during our initial experience with ECMO implants in peripheral hospitals for patients with COVID-19.

RESULTS: During March and April 2020, our team at the University Hospital of Zurich performed 3 out-of-centre ECMO implants at different peripheral hospitals. The implants were performed without any complications. The patients were transported by ambulance or helicopter. Good preparation and selection of the required supplies are the keys to success. The implant should be performed by a well-trained, seasoned ECMO team, because options are limited in most peripheral hospitals.

CONCLUSIONS: Out-of-centre ECMO implants in well-selected patients with COVID-19 is feasible and safe if a well-established organization is available and if the implantation is done by an experienced and regularly trained team.

Keywords: Extracorporeal membrane oxygenation • COVID-19 • Acute respiratory distress syndrome • Pneumonia

ABBREVIATIONS

ARDS	Acute respiratory distress syndrome
COVID-19	Coronavirus disease 2019
ECMO	Extracorporeal membrane oxygenation
ICU	Intensive care unit
V-V	Venovenous
WHO	World Health Organization

INTRODUCTION

Per the current World Health Organization (WHO) figures of 17 April 2000, the new severe acute respiratory syndrome coronavirus 2 has infected >2 million people worldwide with, to date, 139 378 deaths. In Switzerland, the first case of coronavirus disease 2019 (COVID-19) was confirmed on 25 February 2020. To date, a total of 34 000 cases have been confirmed by the health authority in Switzerland [1]. The WHO has declared the disease a Public Health Emergency of International Concern and released interim guidelines on patient management [2]. The WHO interim guidelines made general recommendations for treatment of acute respiratory distress syndrome (ARDS) in patients with COVID-19, including referring patients with refractory hypoxemia to expert centres capable of providing extracorporeal membrane oxygenation (ECMO) therapy. For patients who are not in a conventional transportable condition, we have established a mobile ECMO service so that ECMO therapy can be offered to peripheral hospitals and patients can be transferred safely to a specialized centre for further treatment.

Management of extracorporeal membrane oxygenation in patients with coronavirus disease 2019

All procedures described in this report were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

During March and April 2020, our team at the University Hospital of Zurich performed 3 out-of-centre ECMO implants at different peripheral hospitals. Two out of the 3 centres were already familiar with the principles of ECMO therapy. All patients were men. The median age was 58 years; the youngest patient was 49 years old. Detailed patient characteristics are described in Table 1. All patients were on mechanical ventilation for about 1 week (5–6 days) before respiratory performance, despite an intermittent prone position and high pressure ventilation, rapidly deteriorated further and ECMO became necessary. The median Horowitz index before the ECMO device was implanted was 87 (range 84–93) under FiO2 1.0 and volatile NO therapy in 2 of the patients. Preoperative computed tomography scans were available from all patients, showing the typical ground-glass opacities, consolidations and bronchovascular thickening already described in detail in the literature [3]. One patient had a pneumothorax, which was successfully relieved by a chest drain. For preoperative assessment and evaluation, we developed a specific evaluation sheet for patients with COVID-19 to collect the personal details; age, height and weight; co-morbidities; length of orotracheal intubation and actual ventilation parameters; haemodynamics including catecholamine use; and infection parameters. The PRedicting dEath for SEvere ARDS on VV-ECMO score, the Murray score and the Horowitz index were used to assess the indication and the expected outcome. Although resources may be limited during a pandemic, we gave the priority for ECMO treatment to younger patients with minor or no comorbidities. We formulated in-house indications and contraindications for ECMO in patients with COVID-19 that were discussed by an interdisciplinary team before each implant (Table 2) [4]. The patient's

Table 1: Clinical characteristics and outcomes of out-of-centre extracorporeal membrane oxygenation implants in patients with coronavirus disease 2019 (March–April 2020)

Variables	Patient 1	Patient 2	Patient 3
Age (years)	46	58	59
Sex (male)	x	X	x
Weight/height (kg/cm)	100/181	70/178	140/180
Comorbidities			
• Diabetes		x	
• Hypertension			x
• Adipositas			x
Days before ECMO Implant			
• Onset of symptoms	18	16	17
• Hospital stay	8	11	6
• Mechanical ventilation	5	6	6
Horowitz index before ECMO	87	93	84
Type of ECMO			
• V-V	x	X	x
Cannulation site			
• Right vena jugularis interna	x	x	x
• Right vena femoralis communis	x		x
• Left vena femoralis communis		x	
Perfusion cannula (Fr.)	17	17	19
Drainage cannula (Fr.)	23	23	25
Transport			
• Ground (ambulance)			x
• Air (helicopter)	x	x	
Duration of ECMO (days)	6	9	28
ECMO prognosis	Recovery	Recovery	Recovery

ECMO: extracorporeal membrane oxygenation; Fr.: French; V-V: venovenous.

Table 2: Contraindications for extracorporeal membrane oxygenation in patients infected with coronavirus disease 2019 at the University Hospital of Zurich

Absolute contraindications
• Age >70 years
• Clinical Frailty Scale category ≥3
• Malignant oncological disease in palliative care
• Uncontrolled shock (pH <6.8, lactic acidosis)
• Multiple organ failure
• Moderate to severe neurological impairment
• Moderate to severe cognitive impairment
• Advanced lung disease
• Chronic heart failure (EF <35%)
• Chronic kidney disease (GFR <30)
• Chronic liver failure (child ≥ B)
• Protein-energy malnutrition
• Emergency implantation setting
Relative contraindications
• Obesity BMI ≥35
• No legal medical decision maker available
• Immunocompromised status
• High-dose vasopressor requirement (consider candidate for VA-ECMO)

BMI: body mass index; ECMO: extracorporeal membrane oxygenation; EF: ejection fraction; GFR: glomerular filtration rate; VA: venoarterial.

request and living will must be considered, and the relatives must be actively involved in the decision-making process. Before finally accepting a patient for an out-of-centre ECMO implant and transfer to our intensive care unit (ICU), the local resources were evaluated in detail to make sure optimal care was possible and guaranteed. The best transport routes were identified with the local emergency services before each operation, and the decision was made to use ground or airborne transport (ambulance or helicopter) (Fig. 1A).

Out-of-centre extracorporeal membrane oxygenation team

ECMO therapy is a well-established procedure at our centre in Zurich, with the first implant being performed around 40 years ago. With about 150 ECMO implants per year, our hospital runs one of the leading national ECMO programmes. Within the last 6 years, we performed 165 ECMO transports [5]. During the ongoing COVID-19 pandemic, 9 patients have been supported by ECMO in our hospital so far. All team members are trained on a special ECMO simulator and undergo regular retraining. Thus, we have extensive experience and an existing infrastructure that make it possible to establish such a demanding programme in times of a national crisis.

The mobile ECMO team in our centre comprises a cardiac surgeon, a perfusionist, a rescue doctor and a paramedic. The ECMO equipment is stowed in 5 robust, water-repellent transport bags and can be loaded compactly (Fig. 1B). For the transports, we routinely use the Cardiohelp System (Maquet Getinge AB, Rastatt, Germany) equipped with an HLS 7.0 oxygenator. In case a percutaneous implant is not feasible or complications arise, a complete surgical implant set is available. Upon arrival at the peripheral centre, the ECMO team should take the lead because the colleagues from the peripheral hospitals may not be familiar with the individual details of and supplies needed for an ECMO implant. A case presentation of the patient as well as joint planning of the implant process, with explanation of the individual steps by the surgeon, is essential. Each team member needs to be assigned a role. Before entering the isolated patient room, the cardiac surgeon and the perfusionist select the necessary surgical supplies, based on the size and weight of the patient and the planned ECMO setting [venoarterial or venovenous (V-V) ECMO, cannulation site]. Only supplies that are absolutely necessary for the implant procedure are taken into the isolation area (Table 3). Additional tools that may be required during the operation (additional hydrophilic or stiff wires, catheters, dilators, locks, cannulas, surgical equipment) are provided in front of the isolation area. It is advisable to instruct a local scrub nurse who can prepare further supplies if necessary. All insolation measures must be strictly observed. For the standard V-V ECMO setting, we recommend ultrasound-guided punctures of the right internal jugular and femoral vein. Alternatively, the femorofemoral configuration can be used. Positioning of the cannulas should be done under echocardiographic or fluoroscopic control. For V-V ECMO implants in peripheral hospitals, we prefer ultrasound-guided cannula placement because it is easy to use and available everywhere. Implantation under fluoroscopic control can be challenging, because in our experience not every hospital is equipped with portable fluoroscopy beds on the ICU. Furthermore, moving the patient before ECMO implantation can worsen the haemodynamics and the respiratory situation. The implant should be performed immediately in the ICU, because transporting the patient to the operating room bears the risk of virus transmission to other patients and health care providers while also increasing the risk of environmental contamination. We do not recommend the use of a dual lumen cannula, because the implantation and positioning of the cannula may be time-consuming and require special echocardiographic guidance, which is not always possible in peripheral centres. After the operation, all supplies that have been placed in the isolation area have to be properly disposed of. All team members must be adequately equipped with personal protective equipment (gowns, FFP2/3 mask, glasses, gloves) in accordance with the applicable hygiene regulations and the ability to properly slip in and out of [6]. After arrival at the ECMO centre, the function of the ECMO circuit and the position of the cannula must be checked, because dislocations may occur during transport (Fig. 1C and D). For anticoagulation, unfractionated heparin was used in all patients. Given that the community is aware that COVID-19 may be associated with a hypercoagulable state, we pursue a more aggressive anticoagulation strategy in patients with a target activated clotting time in the upper range (target activated clotting time, 180 s) [7]. Particular caution must be exercised in low-flow situations, which can occur with weaning from ECMO, given the greater risk of ECMO circuit thrombosis.

DISCUSSION

So far there is little information on the use of ECMO in critically ill patients with COVID-19. At the time of this writing, referring to the Extracorporeal Life Support Organization and the Euro Extracorporeal Life Support Organization registry, so far 858 patients with COVID-19 have been supported with ECMO (mean age 52 years; 95% V-V ECMO). In Switzerland, 20 ECMO implants (9 USZ, Zurich; 6 CHUV Lausanne; 3 Inselspital Bern; 2 Basel)

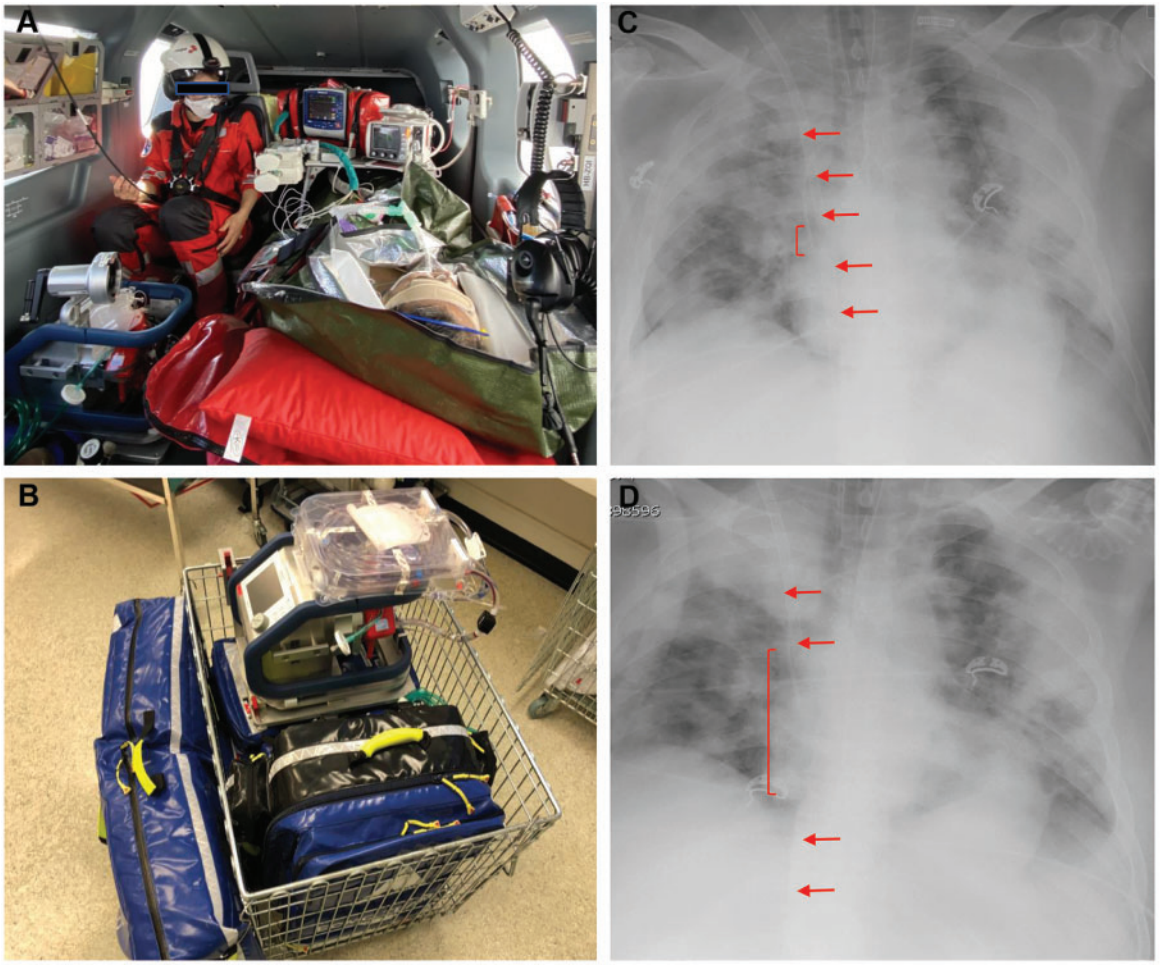

Figure 1: Mobile extracorporeal membrane oxygenation implant equipment. Transportable extracorporeal membrane oxygenation equipment includes 5 transport bags and 1 oxygen cylinder that can be stored compactly (**A**). Transport of a patient with coronavirus disease 2019 on venovenous extracorporeal membrane oxygenation to our university hospital by helicopter (**B**). Post-procedural X-ray and blood gas examination are essential to detect cannula displacement during transfer (**C** and **D**). ECMO: extracorporeal membrane oxygenation.

have been done in this challenging patient group [8]. Most studies are restricted to case reports and small series, reporting a mortality of up to 94% [9]. In patients treated with ECMO for other viral infections causing ARDS, like influenza A (H1N1) in 2009 or the Middle East Respiratory Syndrome Coronavirus in 2012, a decrease in mortality and length of stay in the ICU could be shown, supporting the use of ECMO as a rescue therapy in this population [10, 11]. There is clear evidence of increased mortality with advanced age and comorbidities that should not be overlooked [12]. As the disease burden increases and health systems could reach their limits during a global pandemic, selection criteria should be stringent in order to utilize this valuable resource for those most likely to benefit from this treatment and return to a good quality of life [13].

ECMO is a resource-intensive, highly specialized therapy requiring specially trained doctors and nursing staff. There is some evidence that outcomes from ECMO therapy are better in high volume centres [14]. The role of ECMO in the management of COVID-19 is unclear at this point. Results from prospective studies are currently not available. Should the initial experience with ECMO support in patients with COVID-19 be encouraging, it is likely that non-ECMO centres will refer their patients early to ECMO centres in anticipation of impending clinical deterioration. This procedure will disproportionately affect centres with ECMO programmes, even when ECMO is not required [15]. The transport programme presented can help to avoid this situation, because the experts from the ECMO centre are preoperatively in close contact with the referring clinics and are actively involved in the indication for the ECMO implant. In China, approximately 5% of critically ill patients with COVID-19 have presented rapidly progressive respiratory failure and have developed ARDS [16]. These patients can deteriorate quickly and become unfit for transport to a centre. The ECMO programme presented brings precisely this patient group into a transportable state and enables further care in a higher-level centre. Because any supplies that have entered the isolation area must subsequently be discarded, good preparation and supply selection are key for a safe, successful and resource-saving implant procedure. For ECMO implants in peripheral hospitals, ECMO teams should develop a checklist for cannulation, and team members should ensure they take all necessary supplies with them prior to entering the isolation room. We recommend preparing a cannulation COVID-19 side table that contains all cannulas, extension hoses, connectors, guide wires, fluids, heparin, puncture sets and sterile sleeves needed for the implant procedure. In case additional supplies are needed, a backup bag should be prepared in the clean area

Table 3: Equipment needed for extracorporeal membrane oxygenation implant procedure

Personal protection equipment
• Facemask
• Goggles
• Sterile gowns and gloves
Vascular access kit
• Disinfection kit
• Sterile covers and drapes
• Vascular ultrasound cover and sterile gel
• Local anaesthesia
• Puncture needle
• 20-ml syringe with NaCl
• Sheath (2 × 5 Fr.)
• Standard J-tip working guide wires (80 and 175 cm)
ECMO cannulas
• Drainage cannula (23–25 Fr.)
• Perfusion cannula (17–21 Fr.)
ECMO circuit
• Cardiohelp (Maquet, Getinge AB, Rastatt, Germany)
• HLS 7.0 oxygenator
• Tubing system
• 4 Sterile tubing clamps
• Tubing scissors
• Saline flusher
Surgical instruments
• Scalpel
• Scissors
• Needle holder
• Forceps
• Sutures
• Banding gun with zip ties

ECMO: extracorporeal membrane oxygenation; Fr.: French.

outside the isolation zone. We recommend instructing a dedicated person on the local staff who can provide additional needed equipment for those working in the insolated area.

CONCLUSION

Out-of-centre ECMO implant procedures in well selected patients with COVID-19 are feasible if a well-established organization is available and are safe for both the patient and the personnel. Building up such a programme is time- and resource-consuming and requires specialists from various disciplines. The implant should be performed by a well-trained, seasoned ECMO team, because resources are limited in most peripheral hospitals. Good preparation and selection of the required material are essential. Commissioning new inter-hospital implant and transport programmes for the purposes of treating patients with COVID-19 is therefore not recommended. Centres with already existing transport programmes should plan their operations well, particularly with regard to patient selection, logistics, personnel protection and patient isolation during transport.

Funding

None of the authors received financial support for research, authorship and/or publication of this article.

Conflict of interest: none declared.

Author contributions

Martin O. Schmiady: Data curation; Investigation; Writing—original draft. **Michael Hofmann:** Writing—original draft; Writing—review & editing. **Juri Sromicki:** Writing—review & editing. **Maximilian Halbe:** Data curation; Project administration; Resources. **Koen van Tilburg:** Data curation; Resources. **Raed Aser:** Writing—review & editing. **Carlos A. Mestres:** Validation; Writing—review & editing. **Francesco Maisano:** Supervision. **Enrico Ferrari:** Supervision; Writing—original draft; Writing—review & editing.

Reviewer information

Interactive CardioVascular and Thoracic Surgery thanks Jarle Vaage and the other, anonymous reviewer(s) for their contribution to the peer review process of this article.

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