First Use of a New Extracorporeal Membrane Oxygenation System in COVID19-Associated Adult Respiratory Distress Syndrome: The MobyBox Device

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In late 2020, during the second wave of COVID-19 in Germany, we started using the MobyBox, which is a novel fully pneumatically driven ECMO device, on a regular basis to meet the increasing demand for ECMO therapy. In this case series, we performed a retrospective chart review of seven patients with severe COVID-19-related acute respiratory distress syndrome (ARDS) requiring veno-venous (vv)-ECMO support with the MobyBox. During ECMO treatments we have observed no disadvantages in comparison to conventional ECMO systems. There were no system failures or adverse events directly attributable to the MobyBox system. Our data support that providing vv-ECMO with the MobyBox device is safe and feasible. Furthermore, our findings suggest that the MobyBox device might represent an advantage in terms of biocompatibility. Therefore, more data on this issue is needed to better understand how the pneumatically driven pump affects cellular blood components. *ASAIO Journal* XXX; XX;00–00

Key Words: coronavirus disease 2019, acute respiratory distress syndrome, extracorporeal membrane oxygenation, MobyBox device, pandemic

Introduction

The SARS-Coronavirus 2019 (COVID-19) pandemic placed a huge burden on health care systems all around the world. One common issue was the shortage of treatment capacities in ICU for patients suffering from moderate to severe respiratory failure. During the first wave of COVID-19 in Germany, extensive efforts were made to provide the biggest possible intensive care capacity. Although it was not needed initially, this changed drastically during the second wave in late 2020 and early 2021. Due to a regionally varying incidence of COVID-19 cases, there was a very heterogenous demand for intensive care treatment. In this context, ECMO support in particular for patients with severe respiratory failure proved to be a critical resource.

In late 2020, a North-South gradient of COVID-19 cases in the German federal state of Hessen became obvious, which resulted in fully occupied regional capacities on local intensive care units in southern Hessen. Due to close networking between regional ARDS centers, the leading ARDS center in northern Hessen ("Klinikum Kassel", Hospital in Kassel, Germany) received numerous inquiries to take over patients with severe ARDS for ECMO therapy.

In order to extend our own ECMO capacities in this situation, we decided to start using the new MobyBox ECMO system (Hemovent, Aachen, Germany)[1] for our patients with severe COVID-associated ARDS. The MobyBox ECMO system is a novel, fully pneumatically driven ECMO device, which already demonstrated its feasibility in both veno-venous and veno-arterial modes in an experimental animal model.[2] Common ECMO devices use a power-driven centrifugal pump and a dedicated oxygenator with an additionally added sweep gas flow. In contrast to that, the MobyBox device uses a pneumatically driven pump, which generates a pulsatile flow. The necessary external gas source for the dedicated oxygenator, which is already an integral part of the ECMO circuit, also provides the pressure energy for powering the pump. Therefore, the device does not rely on an external power source, which allows for a significant weight reduction as well as a much more portable design. The actual pump consists of two hemispheric chambers that are interconnected and can operate in a full empty mode. The design of both the pump and oxygenator is based on complete washout (Figure 1).[3] Detailed specifications of the MobyBox device can be found in Table 1, also we added three images of the MobyBox as Supplemental Digital Content 1, http://links.lww.com/ASAIO/A787.

The first use in a patient at our ECMO center was undertaken in late December 2020. In the following weeks of the second and third waves of COVID-19, we used the MobyBox system successfully on several patients.

Methods

During the second wave of COVID-19 (December 2020–January 2021), data were collected from a single center in

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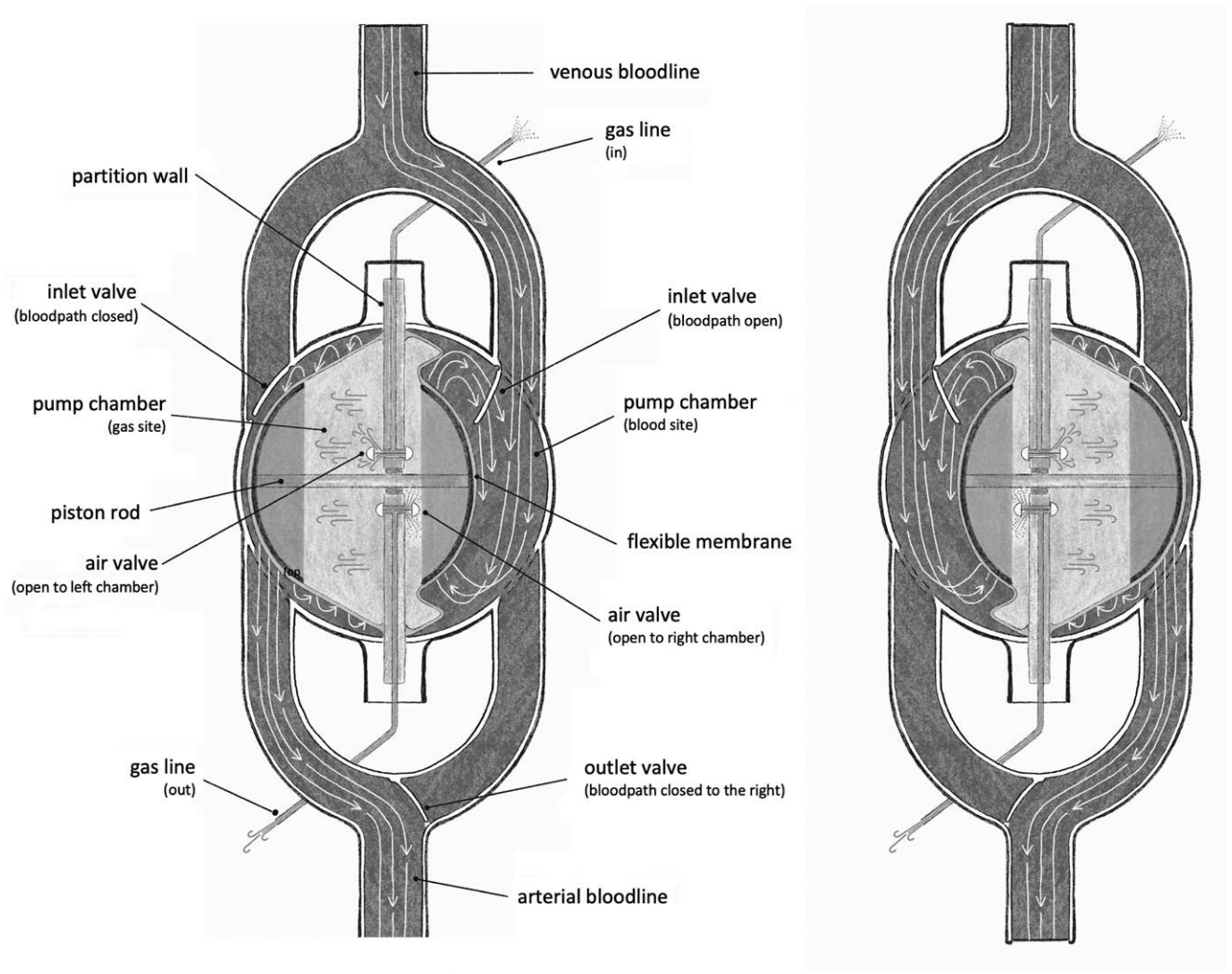

Figure 1. Schematic drawing of the MobyBox device: Working principle of the pneumatic pump including the blood flow. The left and right sides are illustrating the opposite positions of the chamber.

Germany (Intensive Care Unit, Klinikum Kassel). A retrospective approach was chosen focusing on patients that suffered from severe COVID-associated ARDS and required veno-venous ECMO support. Subsequently, we performed a chart review of the first patient cohort that was treated with the new pneumatically driven MobyBox ECMO system (Hemovent, Aachen). The system has a European CE and MDD mark which affirms its conformity with European health, safety, and environmental protection standards for products sold within the European Economic Area and can thus be used in patients.

All members of our ECMO team have been trained and instructed in the use of the MobyBox device so that we could ensure a high level of security. We ensured the availability of a replacement ECMO device at all times in the interest of safety.

This study was approved by the local ethics committee of the Medical Association of the state of Hessen (No. 2020-2099-AF) and was performed according to national law and the declaration of Helsinki.

Patient Population

Between December 20, 2020, and January 31, 2021, a total of seven patients requiring veno-venous ECMO support were treated with the MobyBox ECMO system at our facility. On average, patients were 51.3 years of age (±10.3 years). There were six males and one female.

Five of the COVID-19 related ARDS patients were transferred from other German hospitals, one patient was admitted through our own emergency department. Another patient already had undergone ECMO treatment in an external hospital in Bucharest (Romania).

ECMO Cannulation

At the time of admission to our intensive care unit, all patients were suffering from severe COVID-19 related ARDS. All patients had positive PCR-testing for SARS-CoV2 and radiological features of COVID-19.[4] The mean P_aO_2/F_iO_2-Ratio of the patients before cannulation was 60.6 (±15.7 mm Hg). All patients were invasively ventilated and received standard COVID-19 and ARDS treatment according to the international guidelines including prone positioning and lung-protective ventilation. All patients met the indications for ECMO as stated in the ELSO ECMO guidelines for COVID-19.[5] The mean PEEP before cannulation was 15.2 cm H_2O (±2.9).

Table 1. Device Specifications

Duration of use	Up to 14 days
Shelf life MobyBox System	12 months
Patient unit weight	2.8 kg
Controller unit weight	2.15 kg
Gas interface	Adaptable tube with a diameter from 4–8 mm
Extracorporal circuit interface	3/8"
Gas exchanger filling volume	Approx. 170 ml
Sweep gas flow	0–20 L/min
Priming volume incl. tubing	Approx. 500 ml
Length of blood tubing	2 m each side
Gas exchanger membrane surface	1.6 m^2
Blood flow rate	1–5 L/min at pressure ranges of 0–120 mm Hg at cannula tip location
Max pressure blood side	1.5 bar
Sweep gas flow	0–20 L/min
O_2 transfer rate	100% O_2 saturation at blood flow of 5 L/min, O_2 ≥ 60 ml O_2/min per l/min blood flow
CO_2 transfer rate	≥50 ml CO_2/min per L/min blood flow
Δp gas exchanger blood path	45 mm Hg at 5 L/min blood flow
Δp gas exchanger gas path	10 mm Hg at 20 L/min gas flow

The cannulation of six patients was performed by our ECMO team at referring hospitals before transport. The cannulation procedure was performed according to our protocol with two specially trained clinicians and ultrasound-guided positioning of the cannulas. Five patients had a femoro-femoral configuration, two had a femoro-jugular configuration.

COVID-19 Treatment

After cannulation, all patients received standard treatment according to the German S3-guidelines of COVID-19[6] including low-tidal ventilation, prone positioning, restrictive fluid management, systemic corticosteroid therapy, and adjusted continuous infusion of unfractionated heparin (aPTT 1.5–2.5).

We aimed for a reasonable oxygenation goal with a PaO_2 between 55 and 80 mm Hg or likewise an oxyhaemoglobin saturation between 88 and 95%. The mean arterial pressure target was 60–65 mm Hg if physiologic aims were reached. These included capillary refill time (*i.e.,* warm periphery), sufficient urinary output (≥0.5 ml/kg/h) and normal lactate levels (≤2.0 mmol/L). Norepinephrine was the vasopressor of choice. Transfusions were done in a restrictive manner.

Results

ECMO Support

The overall run-time of the ECMO support was highly variable. Two patients had a long-term requirement with an average of 25.5 days. Three had a mean requirement of 13 days and two required just 5.5 days of ECMO support (Table 2). Overall our patients received an average of 9 days of ECMO support with the MobyBox device. In five of our seven patients, we were able to successfully wean the ECMO support while using the MobyBox device.

Two patients received only MobyBox support at our facility. But one of the two patients had already undergone ECMO treatment at the referring hospital. In all other patients, we performed an inhouse switch from our standard transport system. The switch was necessary due to practical and safety reasons because we intended to continue transferring patients with our conventional ECMO systems. After the switch from our standard transport system to the MobyBox device, we observed no negative effects on the status of our patients. One patient was solely treated with the MobyBox system.

Laboratory Findings

Overall, we observed relatively stable platelet counts and fibrinogen concentrations in patients on MobyBox support (Figure 2). In five of our seven patients, we observed a relative increase in the fibrinogen concentration (Table 3).

All patients required additional blood products. All seven patients received packed red blood cells (PRBC). Moreover, three patients were treated with platelet infusion and four patients received other coagulation products, including factor XIII concentrate, desmopressin acetate, and fibrinogen (Table 4).

Complications

None of the patients showed adverse reactions that could directly be attributed to the MobyBox system. During the treatment, we neither observed the failure of the system nor of its individual components.

Table 2. Patient Demographics

	Patient Number						
	1	2	3	4	5	6	7
Age (y)	54	57	56	30	56	46	60
Sex	Male	Male	Male	Male	Female	Male	Male
Length of Stay on our ICU (day)	61	7	25	22	15	13	29
Duration of MobyBox (day)	19	2	3	4	5	12	18
Duration of ECMO overall (day)	25	6	12	14	5	– *	26
Cannulation sites	V.fem/V.fem	V.fem/V.jug	V.fem/V.fem	V.fem/V.fem	V.fem/V.fem	V.fem/V.fem	V.fem/V.jug
PaO_2/FiO_2 before cannulation	55	52	50	59	90	– *	70
Outcome	†	‡	‡	‡	‡	Ψ	Ψ

*Prior ECMO treatment in Bucharest with unknown date of initial cannulation.
†Died in rehabilitation facility.
‡Discharged from hospital.
ΨDied during ECMO treatment.

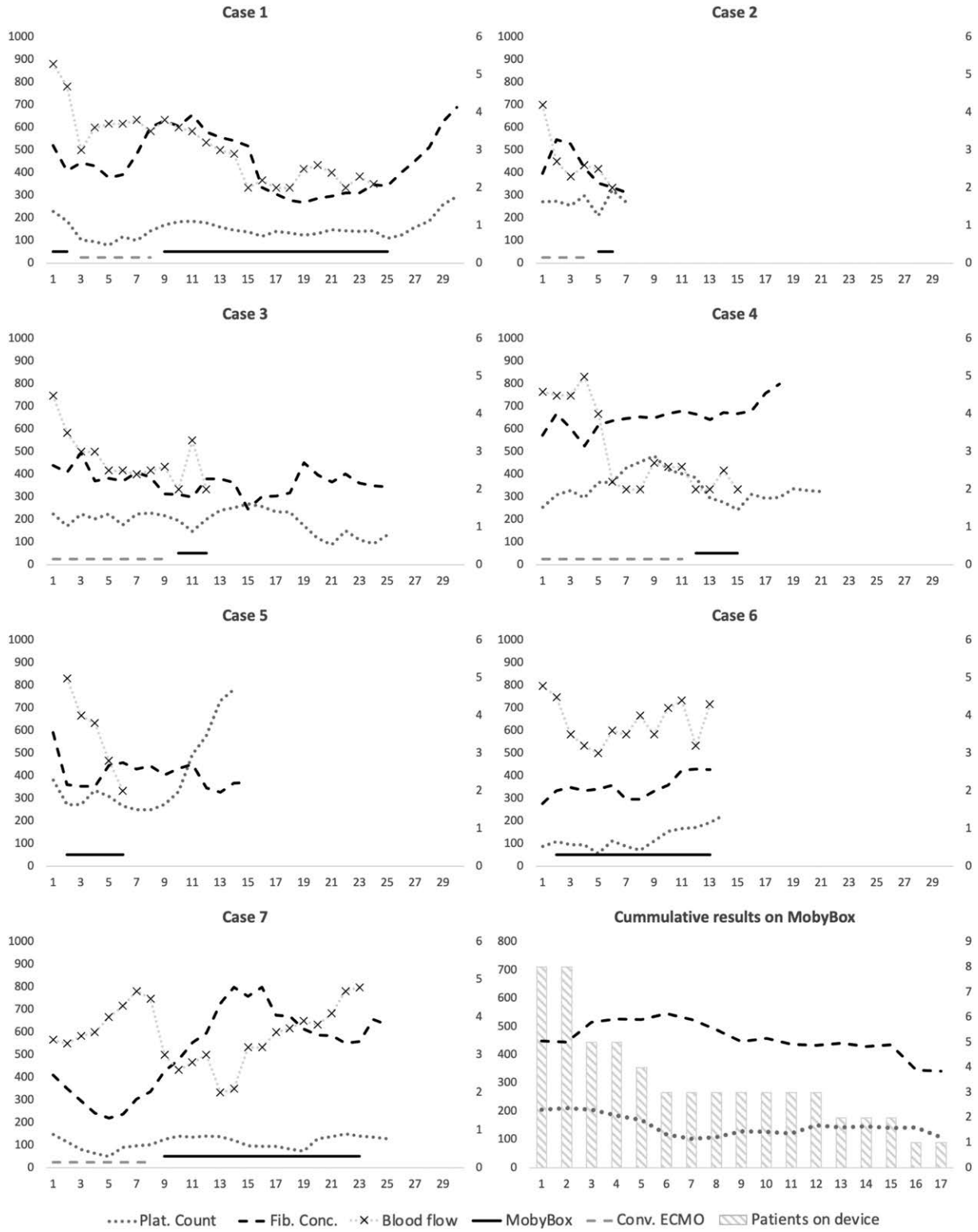

Figure 2. Trajectories of platelet count fibrinogen concentration and blood flow by runtime. Left y-axis: Plat. Count, platelet count (*1000/µl); Fib. Conc., fibrinogen concentration (mg/dl). Right y-axis: ECMO Blood flow (L/min); Patients on device, total count. X-axis: Days of treatment with runtimes of ECMO devices marked on the bottom. MobyBox, marks runtime of the MobyBox device; Conv. ECMO, marks runtime of conventional ECMO devices.

One of the seven patients developed a major bleeding at the ECMO cannula sites and epistaxis. Another patient developed a thrombotic event. However, this could not be directly related to the MobyBox system as it had been a result of a preceding arterial catherization in the Arteria radialis and the COVID-disease.

Table 3. Increase/Decrease of Platelet Counts and Fibrinogen Concentration

	Run Number*							
	1†	2†	3	4	5	6	7	8
Runtime (day)	2	17	2	2	4	5	12	15
Change of platelet count (%)‡	−18.86	−35.88	+55.02	+35.81	−36.95	−1.48	+74.55	+12.80
Change of fibrinogen concentration (%)‡	−21.84	−45.64	−5.35	+27.09	+0.30	+26.87	+27.68	+30.54

*One patient had two treatments with the MobyBox device. Therefore, the total count of runs is eight.
†Same patient.
‡Calculated was the difference between the first and the last value of platelet count and fibrinogen concentration for each treatment with the MobyBox device.

Outcome

Five of the seven patients improved clinically to the point that they could finally be weaned from the ECMO support and returned to more conventional intensive care management. Four patients have already been discharged from the hospital. Two patients died of COVID-19 during treatment at our facility. One patient died in an external rehabilitation facility.

Discussion

The presented case series outlines the use of the MobyBox ECMO system in patients suffering from severe COVID-19 related ARDS during the COVID-19 pandemic. We have successfully demonstrated the safety and feasibility of this novel pneumatically driven biventricular displacement pump.

During treatment, we could not observe any disadvantages compared to our conventionally used ECMO systems. In six of our seven patients, we performed a switch from a common centrifugal ECMO device to the MobyBox. Afterwards, we have observed no negative effects of this switch in any of these patients.

The MobyBox is currently licensed for a duration of use of up to 14 days. According to the manufacturer, there is no technical reason for this limitation and it is only because of the duration of the clinical trials used for the certification process. However, when exceeding this limit in two of our patients we did not observe any differences in the treatment, complications or other issues.

Throughout the treatment phase, no system failures or adverse events could directly be attributed to the MobyBox device. Furthermore, no thrombotic events (including circuit thrombosis) were observed.

It is common practice to interpret the loss of platelets as a hallmark for ECMO systems because of their leading role in bleeding complications. Therefore, platelets have been accepted as a marker for biocompatibility equally as the loss of fibrinogen.

Karagiannidis *et al*. have demonstrated steady platelet counts and rising fibrinogen concentrations during ECMO support with the MobyBox in sheep.[3] They have claimed that the new blood pump with its washout behavior was associated with a short-term drop in platelets at the beginning of the treatment, but that the platelet levels rapidly recovered. Furthermore, there was no drop in the fibrinogen after a slight increase on day one of the treatment. Based on this, we performed our own retrospective analysis of the platelet counts and fibrinogen concentration. We have also demonstrated stable platelet counts and no fibrinogen loss.

This is of major importance because this could be an indicator of biocompatibility of the MobyBox device. Falling concentrations of fibrinogen are a sign of hemolysis related to microthrombosis of the oxygenator. Hemolysis is one of the major complications and an independent risk factor associated with death during ECMO treatment. A possible reason for this might be the design of the MobyBox device. Both pump and oxygenator have been designed for an optimized washout. Additionally, the noncontinuous flow conditions of the novel pump principle avoid stagnant flow areas prone to blood clotting within the entire external circuit. The overlaying pulse within the oxygenator could also have a beneficial effect on the blood to fiber interaction resulting in a higher gas transfer efficiency. Furthermore, the displacement pump creates lower shear stress on blood components in comparison to conventional rotating pumps.

With this, one must also keep in mind that all patients were suffering from COVID-associated ARDS and some required infusion of platelets and coagulation products *e.g.* fibrinogen. However, we were able to demonstrate some promising similarities to the findings of Karagiannidis *et al*.[3]

This case series has several limitations. Both, the small number of cases and the heterogenous progress of the disease

Table 4. Cumulative Total of Blood Products Required for ECMO Run

	Patient Number						
	1	2	3	4	5	6	7
PRBC							
ml/kg body weight*	74.25	3.24	21.39	5.50	11.34	67.22	52.25
Units/day	1.08	0.17	0.58	0.14	0.8	1.69	0.73
Platelets							
ml/kg body weight*	17.50	–	–	–	–	27.78	22.50
Units/day	0.24	–	–	–	–	0.77	0.35

*Assumed mean volumes: PRBC 275 ml, platelets 250 ml.

do not allow for statistical analysis regarding this issue. Furthermore, there were significant differences in the runtimes of ECMO support. Therefore, more data on this issue is needed to better understand the effects that the MobyBox system has on blood components in comparison to conventional rotating pumps.

Conclusion

The on-hand case series is the first one to describe the successful use of the MobyBox ECMO device (Hemovent, Aachen, Germany) in patients suffering from severe COVID-19 related ARDS. In this limited series of patients, the MobyBox proved to be safe and effective in the management of respiratory failure. These findings suggest that MobyBox is a suitable alternative to the established ECMO devices with power-driven centrifugal pumps. In addition, our findings suggest that the MobyBox device may provide an advantage in terms of biocompatibility.

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