



## Case report

# Idiopathic pulmonary fibrosis patient supported with extracorporeal membrane oxygenation for 403 days while waiting for a lung transplant: A case report

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## ABSTRACT

According to the Extracorporeal Life Support Organization, the average duration of veno-venous extracorporeal membrane oxygenation (V-V ECMO) in adults with acute respiratory failure is 10.5–13.5 days. Some patients on V-V ECMO may not recover in such a short period of time, and recently, there have been more reports of prolonged V-V ECMO. However, we do not know how long it is feasible to wait for native lung recovery or lung transplant (LTx) with the use of ECMO. We describe a patient with acute exacerbation of idiopathic pulmonary fibrosis supported by ECMO for 403 days while waiting for a LTx. In this case, we kept the patient awake, and he was communicating frequently with his family. We changed the membrane oxygenator 23 times and the cannula 10 times without complication. However, we terminated the treatment on day 403 of ECMO because there was no access site for cannula insertion due to blockage by a venous thrombotic occlusion, making it impossible to continue this bridge to lung transplantation. It has become possible to maintain patients on ECMO for extended periods of time, but it is difficult to manage ECMO for more than one year without the development of a more durable lung support system.

## 1. Introduction

The use of veno-venous extracorporeal membrane oxygenation (V-V ECMO) has been increasing as a supportive approach during recovery of patients with severe acute respiratory failure that is refractory to conventional mechanical ventilation or while waiting for lung transplantation (LTx). According to the 2016 Extracorporeal Life Support Organization (ELSO) registry report, the average duration of V-V ECMO in adults with acute respiratory failure is 10.5–13.5 days [1]. Some patients whose lung damage is not improved may require support of V-V ECMO for more than 2 weeks, and recently, there have been more reports of prolonged V-V ECMO [2–8]. However, we do not know how long it is feasible to wait for native lung recovery or lung transplant (LTx) with the use of ECMO. We describe a case of idiopathic pulmonary fibrosis in which a patient was supported by ECMO for 403 days while waiting for a LTx.

## 2. Case report

A 50-year-old Japanese man with a history of idiopathic pulmonary

fibrosis was transported to a hospital in Singapore from Indonesia because of hypoxia that had begun 8 days previously. Acute exacerbation of idiopathic pulmonary fibrosis was diagnosed. Broad-spectrum antibiotics and prednisolone were administered. However, his clinical condition started to deteriorate; he was subsequently intubated and mechanically ventilated. Despite aggressive mechanical ventilation, partial pressure of arterial carbon dioxide (PaCO<sub>2</sub>) was 88 mmHg and partial pressure of arterial oxygen (PaO<sub>2</sub>) was 48 mmHg with fraction of inspired oxygen (FIO<sub>2</sub>) of 1.0. Therefore, it was decided to place him on V-V ECMO (Cardiohelp system, Maquet Cardiopulmonary, Hirrlingen, Germany). A 21-Fr drainage cannula was inserted in the left femoral vein, and a 19-Fr return cannula was inserted in the right femoral vein (HLS Cannula Maquet Cardiopulmonary, Hirrlingen, Germany). After initiation of ECMO, his condition stabilized, and a tracheostomy was performed. However, he did not show any improvement and did not have the right to undergo LTx in Singapore because of legal issues. For this reason, he was transported to our intensive care unit (ICU) in Japan.

Upon admission to our ICU, he was sedated and mechanically ventilated. We controlled ECMO blood flow around 4 L/min, to

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maintain peripheral capillary oxygen saturation (SpO<sub>2</sub>) over 85%, and sweep gas flow with 100% of oxygen through a membrane oxygenator, to maintain PaCO<sub>2</sub> between 30 mmHg and 35 mmHg. The mechanical ventilation settings were altered to a “lung rest” setting, which consisted of a driving pressure of 5 cmH<sub>2</sub>O, positive end-expiratory pressure of 10 cmH<sub>2</sub>O, and FIO<sub>2</sub> of 0.4. With regard to hemodynamics, his heart rate was 50 beats/min and blood pressure was 156/104 mmHg without an inotrope. Echocardiography revealed an ejection fraction of 60.7% and a tricuspid regurgitation pressure gradient (TR-PG) of 10 mmHg. His renal function was normal. He was administered anticoagulant with heparin to maintain an activated partial thromboplastin time between 50 and 80 seconds. Vancomycin prophylaxis, used in this case, is routinely prescribed for patients on long-term ECMO. This drug regimen has been the standard of care in our institution and was adapted in accordance with a prior publication [9]. Other antibiotics were administered as required based on the laboratory data from bacterial cultures.

His condition then gradually improved. The mechanical ventilation was discontinued on day 38. Once he was awake, we removed his tracheostomy tube and replaced it with a speech cannula on day 42. After the application of a speech cannula and its subsequent removal, the patient was administered low-flow or high-flow oxygen therapy with a nasal cannula or Venturi mask, as required to maintain the SpO<sub>2</sub> greater than 85%, under sufficient ECMO support. Oral intake began on day 47. Severe respiratory failure persisted, but none of his other organ systems failed. Target SpO<sub>2</sub> and PaCO<sub>2</sub> values were achieved by fine adjustment of ECMO blood flow, sweep gas flow through the membrane oxygenator, and supplemental oxygen through his native lung; in addition, analgesia was induced by the administration of morphine as required. He was fully awake, oriented, and communicative, and was seen daily by a physiotherapist for exercise and respiratory training. We made a clinical decision that the patient's respiratory failure was irreversible and that he should be listed on the LTx registry. We consulted the LTx center for LTx evaluation on day 59. While awaiting LTx, we changed the membrane oxygenator 23 times and the cannula 10 times. We changed the oxygenator because of gas exchange failure, apparent thrombus on the membrane, and acute platelet reduction due to massive clot formation around the hollow-fiber bundles in the oxygenator. The average lifespan of the oxygenators was 16 days. We also changed the cannula when the patient was clinically diagnosed with sepsis because of blood stream infection caused by indwelling artificial instruments in the major vessels. As the double lumen cannula was not available in our country, two-site cannulation mode was necessary for V-V ECMO. We used the right internal jugular vein for drainage four times, the right femoral vein for drainage four times, and the left femoral vein for drainage three times. We used the left internal jugular vein for return three times, the right femoral vein for return three times, and the left femoral vein for return one time. We typically inserted a 25 or 23-Fr cannula for drainage and a 23 or 21-Fr cannula for return. There were no technical complications.

On day 223, the patient complained of dyspnea. His SpO<sub>2</sub> was around 90% on ECMO with a flow of 5 L/min. Echocardiography showed a D shape, and the TR-PG was 56 mmHg; it had been 27 mmHg on day 201. We administered the endothelin-receptor antagonist bosentan, and the phosphodiesterase type 5 inhibitor sildenafil; however, his right failure became worse, and TR-PG increased to 78 mmHg on day 226. We made the decision to convert the configuration of ECMO from V-V to venovenous-arterial (VV-A). After this conversion, his condition improved, and TR-PG decreased to 43 mmHg. On day 282, his ECMO configuration was converted from VV-A back to V-V, and on day 284, he was finally listed on the LTx registry.

On day 305, we attempted to change the cannula to prevent cannula-related blood stream infection. However, his remaining veins were occluded by thrombosis, and we could not access them to modify the site of cannulation. Therefore, we used the same cannula that was inserted on day 276. On day 371, he went into septic shock; thus, we

attempted to change the cannula again. We checked each vein by echocardiography and discovered that there was no flow in any of them. Despite the situation, the patient was relatively stable; he could talk and was able to maintain oral intake. However, we decided not to continue ECMO support. We disconnected him from ECMO on day 403 of ECMO and the patient died soon thereafter. An autopsy was not performed because we could not obtain consent from the next-of-kin.

### 3. Discussion

We managed a patient with acute exacerbation of idiopathic pulmonary fibrosis on ECMO in an awake state for approximately 1 year without life-threatening complications. Although device improvements have allowed for longer ECMO support, we hypothesize that the maximum duration is limited to 1 year because of destruction of the access site, pulmonary hypertension, and infection.

Several other authors have also reported prolonged V-V ECMO with native lung recovery [2–8]. Akkanti et al. reported a case of a 30-year-old man with influenza A who was weaned off V-V ECMO after 193 days and was ambulatory at discharge from the hospital [2]. Wiktor et al. reported a 40-year-old woman who was supported by V-V ECMO for 265 days but died 4 days later [3]. According to the ELSO, the longest duration of ECMO is 315 days [10]. Therefore, this report is the longest duration of ECMO, although we could not prolong the duration until LTx could be performed. It has become possible to maintain patients on ECMO over a long period of time not only because of device improvements but also because of comprehensive management such as maintaining the patient's ability to remain awake and communicate with family, as well as oral ingestion and rehabilitation. It is always difficult for medical staff to decide to terminate the life of patients who are waiting for LTx and express the desire to live just because the cost is high or ECMO maintenance is labor intensive. However, we believe there is a limit to the duration of ECMO.

The survival rate of prolonged-ECMO (> 14 days) for adults with respiratory failure is lower than the survival rate of adults who require short duration ECMO (< 14 days) [11]. The prolonged use of ECMO (> 28 days) in children with refractory cardiac failure, respiratory failure, or both is associated with a low survival rate and a high rate of complications [12]. Furthermore, the duration of ECMO is associated with nosocomial infection [13]. In the ELSO guidelines, an example is given of stopping support in cases where it is futile to prolong the duration of ECMO, for example, if 2 weeks of no lung function and fixed pulmonary hypertension are documented in a patient who is not a transplant candidate [14].

Akkanti et al. and Wiktor et al. reported their patient had decreased right ventricular systolic function during prolonged ECMO therapy [2,3]. If pulmonary hypertension and right ventricular dysfunction does not improve, withdrawing ECMO support may be considered. In the present case, pulmonary hypertension developed after approximately 7 months; that may have been the appropriate time to withdraw ECMO support, if we had not been waiting for LTx.

The main reason we decided to withdraw ECMO therapy was destruction of the access site, which made it impossible to continue ECMO support while continuing to wait for LTx. There exists a high incidence of venous thrombosis during and after ECMO. Placement of large-size cannula in the jugular or femoral veins has been associated with endothelial damage and low flow, which may cause a clot [15,16]. Periodic cannula replacement is necessary to avoid septic shock, although frequent cannulation may be one reason that ECMO support cannot continue indefinitely.

Organ allocation for LTx is currently determined by the severity of the disease and the predicted post-transplant survival in the US and Europe [17,18]. Therefore, several patients receiving ECMO have undergone LTx [19–22]. However, in some countries in which LTx is not based on medical urgency, patients on ECMO who must wait for an extended period for donor lungs might not achieve a successful LTx.

LTx candidates typically wait 2.5–3 years after being listed on the LTx registry in Japan. Only one ECMO patient has successfully bridged to LTx [23]. Crotti et al. reported that the duration of ECMO support while awaiting LTx affects morbidity and mortality [24]. The possible duration of ECMO support has only been extended by some months, which suggests that patients requiring ECMO support should be moved to the top of the list as urgent recipients. Without an allocation system in which patients on ECMO are prioritized to undergo LTx, we may have to consider candidates of ECMO more seriously before initiating ECMO, not only because of low PaO<sub>2</sub>/FIO<sub>2</sub> ratio, but also primary diagnosis or age.

We acknowledge there are several limitations in this study. Wiktor et al. reported that they used Avalon bicaval cannula without exchange for 230 days [3]. We may be able to support a patient longer using this type of cannula. However, we believe that the occasional exchange of cannula was mandatory to cope with blood stream infection related to cannula in the vessels.

To summarize, we supported a patient on ECMO without mechanical complications by precise management for approximately 1 year. There are difficulties associated with waiting for LTx or recovery of more than 1 year. The development of an artificial lung that can function for a long duration, and a cannula to avoid thrombus formation are required.

## Consent

Written informed consent was obtained from the patient's family for publication of this case report.

## Conflict-of-interest statement

The authors declare no conflicts of interest.

## Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.rmcr.2018.04.015>.

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