Extracorporeal Membrane Oxygenation in Pulmonary Crisis and Primary Graft Dysfunction

Hsao-Hsun Hsu, MD, Wen-Je Ko, MD, PhD, Jin-Shing Chen, MD, PhD, Cheng-Hsin Lin, MD, Shuenn-Wen Kuo, MD, Shu-Chien Huang, MD, and Yung-Chie Lee, MD, PhD

This report describes the clinical use of an extracorporeal membrane oxygenation system in a 23-year-old woman with severe pulmonary arterial hypertension due to end-stage systemic lupus erythematosus. The system was also used to provide a direct bridge from resuscitation to transplantation after acute onset of pulmonary crisis and maintenance of stable hemodynamics during the bilateral lung transplant, and also to provide optimal oxygenation until the transplanted lung recovered from severe primary graft dysfunction. J Heart Lung Transplant 2008;27:233–7. Copyright © 2008 by the International Society for Heart and Lung Transplantation.

Extracorporeal membrane oxygenation (ECMO), which involves gas exchange through an extracorporeal oxygenator, provides both oxygenation and carbon dioxide removal. It can also be as a temporary lung assistance device for waitlisted patients with acute hemodynamic collapse, bridging the gap until lung transplantation (LTx) can be accomplished. In addition, varying the ECMO circuit settings is an excellent approach to stabilizing patient hemodynamics during LTx, replacing cardiopulmonary bypass (CPB). Primary graft dysfunction (PGD), also referred to as ischemia–reperfusion injury, remains a major complication that contributes significantly to early post-transplant mortality. When PGD is so severe that oxygenation cannot be maintained despite optimal conventional therapy, ECMO helps restore adequate perfusion and gas exchange and allows for a period of relative lung rest until recovery.

Herein we report utilization of different ECMO circuit settings to successfully rescue a female patient with systemic lupus erythematosus (SLE) in acute pulmonary crisis. Furthermore, continuation of this support provided a therapeutic bridge until bilateral lung transplantation (BLTx) from a marginal donor could be performed, and hemodynamic stabilization to allow lung graft recovery from severe post-transplant primary graft failure.

METHODS

Our patient was a 23-year-old woman with SLE. Three years earlier, at 20 years of age, she was diagnosed with severe pulmonary arterial hypertension (PAH). Because her symptoms of PAH progressed and remained unresponsive to optimal medical treatment, she was referred to our hospital for lung transplantation. However, right heart failure worsened quickly and acute pulmonary crisis occurred suddenly during admission. Emergency lifesaving venovenous (V-V) ECMO cannulation through the superior vena cava (SVC) and inferior vena cava (IVC) was performed (Figure 1A). The ECMO circuit consisted of a centrifugal pump, a hollow-fiber microporous membrane oxygenator and percutaneous thin-wall cannulae (Medtronic, Inc., Anaheim, CA), all of which were coated with a heparin-bound Carmeda Bioactive surface. Low-dose heparin was infused to keep activated clotting time (ACT) at 160 to 180 seconds. The pulmonary hypoxia and hemodynamic compromise rapidly improved and the PaO2/FIO2 ratio of the arterial blood in the radial artery increased from 52 to 127 mm Hg. After 15 days of V-V ECMO life support, the patient underwent BLTx using a marginal donor whose arterial blood PaO2/FIO2 ratio was 280 mm Hg before organ procurement.

After clamshell incision, V-V ECMO was converted to VVV-A (veno-veno-venoarterial) ECMO, a variant of venoarterial (V-A) ECMO, prior to BLTx (Figure 1B). The VVV-A ECMO circuit consisted of a centrifugal pump, a hollow-fiber microporous membrane oxygenator and percutaneous thin-wall cannulae (Medtronic, Inc., Anaheim, CA), all of which were coated with a heparin-bound Carmeda Bioactive surface. Low-dose heparin was infused to keep activated clotting time (ACT) at 160 to 180 seconds. The pulmonary hypoxia and hemodynamic compromise rapidly improved and the PaO2/FIO2 ratio of the arterial blood in the radial artery increased from 52 to 127 mm Hg. After 15 days of V-V ECMO life support, the patient underwent BLTx using a marginal donor whose arterial blood PaO2/FIO2 ratio was 280 mm Hg before organ procurement.

From the *Department of Surgery, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan; **Department of Surgery, Chi-Mei Medical Center, Tainan, Taiwan; and *Department of Traumatology, National Taiwan University Hospital and University College of Medicine, Taipei, Taiwan.

Submitted July 23, 2007; revised October 26, 2007; accepted November 26, 2007.

Reprint requests: Yung-Chie Lee, MD, Department of Surgery, National Taiwan University Hospital, No. 7, Chung-Shan South Road, Taipei 100, Taiwan. Telephone: 886-2-23123456 (ext. 5070). Fax: 886-2-23412542. E-mail: yclee@ntuh.gov.tw.

Copyright © 2008 by the International Society for Heart and Lung Transplantation. 1053-2498/08/$–see front matter. doi:10.1016/j.healun.2007.11.570

233
donor lung, the BLTx proceeded uneventfully with a total ischemia time of 6 hours. The MPA and aortic arch cannula were then removed post-transplant, and the ECMO system was converted to the veno-venoarterial (VV-A) setting, a variant of V-A ECMO, due to unsatisfactory oxygenation and unstable hemodynamics caused by the severe PGD (Figure 1C). The VV-A circuit drained the blood from the SVC and IVC, perfusing the well-oxygenated blood into the right femoral artery through a new cannula (Tube e). The patient was subsequently

Figure 1. Four types of extracorporeal membrane oxygenation (ECMO) circuit and cannula placement. (A) Venovenous (V-V) ECMO circuit for pulmonary crisis before bilateral lung transplant (BLTx). The drainage cannula (Tube a) passes down the right femoral vein to the inferior vena cava (IVC). The perfusion cannula (Tube b) passes down from the right internal jugular vein to the superior vena cava (SVC). (B) Veno-veno-venoarterial (VVV-A) ECMO circuit during BLTx. Blood drains from SVC, IVC and main pulmonary artery (Tubes b, a and c, respectively). The oxygenated blood is returned through the cannula inserted into the aortic arch (Tube d). (C) Veno-veno-arterial (VV-A) ECMO circuit immediately after BLTx. The blood drains from the SVC and IVC and returns through the cannula inserted into the right femoral artery (Tubes b, a, and e, respectively). (D) Veno-arteriovenous (V-AV) ECMO circuit for severe primary graft dysfunction. The blood drains from the right femoral artery (Tube e), with the oxygenated blood returning equally through the SVC (Tube b) and right femoral artery (Tube e) using an extra roller pump on the latter.
sent to the intensive care unit (ICU) for post-operative care.

RESULTS
Although under VV-A ECMO support with inhaled nitric oxide and vasodilators, the PGD was so severe that the PaO₂/FIO₂ ratio deteriorated from 80 mm Hg immediately after the operation to 45 mm Hg on post-operative day (POD) 1. The tidal volume also decreased from 250 to 150 ml under pressure-controlled ventilation at inspiratory and positive end-expiratory pressures of 25 and 10 cm H₂O, respectively. The chest radiograph (CXR) showed diffuse opacification in all quadrants (Figure 2A).

Because the hypoxemia in the upper body was too severe to support only V-A ECMO, V-AV ECMO, a variant of the combined V-V and V-A ECMO system, was applied to improve the upper-body hypoxia (Figure 1D). V-AV ECMO drained blood from the IVC and the arterialized blood return distributed almost equally into the SVC (Cannula b) and right femoral artery (Cannula e), with an additional roller pump (COBE International, Arvada, CO) used to control blood flow in the latter. The PaO₂/FIO₂ ratio in the radial arterial blood rapidly increased from 45 to 98 mm Hg after V-AV ECMO was commenced, and the hemodynamics were stabilized. On POD 9, the PaO₂/FIO₂ ratio had increased to 246 mm Hg and the tidal volume increased to 330 ml, with the CXR revealing a prompt reduction in pulmonary opacification. The patient was successfully weaned from the ECMO system on POD 9. Follow-up CXR revealed an almost clear lung field 8 weeks post-transplant (Figure 2B). The patient was subsequently discharged without complications and is alive and well 12 months after the operation.

DISCUSSION
The mean reported duration of survival from PAH onset in SLE patients is <2 years and LTx should be considered in severe or progressive impairment due to PAH. Acute pulmonary crisis was one of the major causes of death in critical patients, even in those who were already listed for LTx. Criteria for implementing ECMO in PAH patients included acute pulmonary crisis, progressive hypoxemia despite optimized ventilatory support, high peak airway pressures, poor response to inhaled nitric oxide, falling venous saturation and high-dose vasopressor requirements. VV ECMO might reasonably be expected to be efficacious in acute pulmonary crises because it can directly infuse well-oxygenated blood into the right heart and quickly raise arterial oxygen tension in the pulmonary circulation, dilate the pulmonary vessels, and then decrease the pulmonary arterial pressure. Furthermore, ECMO may also provide lifesaving temporary support in such critical situations until an organ becomes available for LTx.

Aigner et al reported two cases of using ECMO as a bridge to LTx from their 306 LTx patients in the course of 5 years. Both patients required ECMO due to inadequate gas exchange under conventional respira-
tory therapy before LTx. ECMO was continued intraoperatively and post-operatively prolonged. Although both patients were weaned off ECMO successfully, only one patient survived for >2 months post-operatively.

Due to the unstable and irreversible preceding hemodynamic decompensation in PAH patients with pulmonary crisis, urgent LTx was the recommended treatment choice. However, the lack of organ donors is most serious for patients awaiting LTx in Taiwan. According to a report from the Taiwan Organ Registry Sharing Center, the average annual number of LTx procedures in the past 5 years was only seven, due to the scarcity of lung donors. Although half of the LTx procedures were performed by our surgical team, the majority of our listed patients waited >10 months before receiving a LTx. Therefore, aggressive use of marginal donors (arterial blood PaO₂/FIO₂ ratio >250 mm Hg) has helped to relieve the shortage of compatible donor organs and decrease critical waitlist mortality.

Because increasing pulmonary artery pressure (PAP) is a risk factor for 90-day mortality after single LTx, BLTx is preferred in patients with severe PAH. It is usually performed while on CPB, which provides intraoperative hemodynamic stability and avoids initial over-flow of the first implanted lung during the second lung transplant. However, CPB is associated with a higher incidence of peri-operative complications due to the requirement of full systemic anti-coagulation and high blood turnover in the suction system, which results in recirculation of activated inflammatory mediators.

As described herein, pre-operative V-V ECMO can easily be switched to a VVV-A circuit intra-operatively, replacing CPB and improving patient tolerance to the BLTx procedure. In our VVV-A circuit, the inclusion of an extra cannula to drain blood from the MPA not only avoids exposing the first implanted lung to the entire cardiac output during implantation of the second organ, but it also facilitates the subsequent arterial anastomosis despite the obvious size discrepancy between donor and recipient pulmonary arteries. Fully oxygenated blood can also be perfused through the aortic cannula to the vital organs during the transplant with efficacy comparable to CPB. Most importantly, because heparin-bound tubing is utilized in our ECMO circuit, systemic heparinization is not required intra-operatively. In contrast, in CPB, it frequently leads to post-operative intra-thoracic bleeding in recipients with strong adherence between the lung and inner thoracic wall.

Despite all efforts, some patients may still experience severe PGD refractory to mechanical ventilation, nitric oxide, prostaglandin infusion and unconventional modes of respiratory support. When PGD remains unresponsive to maximal conventional management, ECMO can support gas exchange and stabilize the patient’s condition until the lungs recover. The V-V ECMO system has the theoretical advantage of perfusing most oxygenated blood directly to the right heart, providing optimal oxygen tension in the pulmonary circulation. By contrast, although V-A ECMO can provide support during both cardiac failure and respiratory failure, femoral V-A ECMO does not relieve severe hypoxemia in the upper body during severe oxygenation failure. Therefore, when V-A ECMO cannot sustain adequate oxygenation in the upper body and stabilize hemodynamics caused by severe PGD, another V-V ECMO circuit may be added. It appears reasonable to suggest, however, that two ECMO circuits constitute too much systemic invasion, without even taking into account the organizational overhead associated with system maintenance and labor requirements.

By comparison, the described V-AV ECMO system offers functionality and efficacy comparable to V-V and V-A ECMO while providing the combined benefits of both. This V-AV system uses the same number of cannulae as VV-A ECMO (n = 3), with the only modification being a simple change in direction of blood flow in Tube b. An additional roller pump controls the blood flow, providing equal distribution into the arterial and venous circulation. This new ECMO setting works well and provides adequate gas exchange while allowing the patient to tolerate severe PGD without damage to other vital organs. To the best of our knowledge, using this V-AV ECMO model to maintain adequate oxygenation and stable hemodynamics in patients with severe PGD after LTx has not been reported.

In conclusion, although this technique is somewhat labor intensive, requires more capital equipment, and has a higher operational cost, the ECMO system described herein offers a number of potentially lifesaving advantages in critical cases. Our SLE patient in pulmonary crisis was successfully resuscitated using ECMO, and then it was used to provide bridging until a marginal organ was available, tolerance to the BLTx procedure despite sub-optimal compatibility, and transplant graft recovery from severe PGD post-operatively.

REFERENCES


