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# Successful Recovery After Veno-Arterio-Venous Extracorporeal Membrane Oxygenation Immediately Before Liver Transplantation in Multi-Organ Failure Including Acute Respiratory Distress Syndrome: A Case Report

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## ABSTRACT

Extracorporeal membrane oxygenation (ECMO) has emerged as an alternative treatment to conventional ventilation maneuvers in the nontransplantation literature to support acute respiratory distress syndrome. However, the role of ECMO in transplant is unclear, and few case reports have described using ECMO pretransplant. We discuss the successful use of veno-arteriovenous ECMO as a bridge therapy to deceased donor liver transplant (LT) in acute respiratory distress syndrome. Because the incidence of severe pulmonary complications resulting in acute respiratory distress syndrome with multiorgan failure is rare before LT, determining the usefulness of ECMO is challenging. However, in acute but reversible respiratory failure and cardiovascular failure, veno-arteriovenous ECMO provides a useful therapeutic option as a bridge for patients awaiting LT and should be considered if available even in multiorgan failure.

**E**XTRACORPOREAL membrane oxygenation (ECMO) can be used as a salvage maneuver in patients with severe respiratory failure in whom conventional ventilation has proven inadequate [1]. Although the indications and role of ECMO in the nontransplantation literature are established, the role of ECMO in transplant is unclear.

Acute respiratory distress syndrome (ARDS) is a clinical syndrome presenting with rapidly progressed noncardiac hypoxemia after an insult [2]. Although enormous resources have been invested in basic and clinical research on ARDS, its associated mortality remains very high [3].

Extracorporeal membrane oxygenation has emerged as an alternative treatment to conventional ventilation maneuvers in the non-transplant literature to support ARDS. The Conventional Versus ECMO for Severe Adult Respiratory Failure trial in the United Kingdom was a randomized control trial comparing the management of severe ARDS (Murray score >3 or pH < 7.20) with conventional ventilation vs referral for treatment using ECMO. The 6-month survival without disability using ECMO was 63% vs 47% in the conventional arm [4]. Based on these findings, referral for management offering ECMO

treatment was recommended for adult patients with severe but potentially reversible respiratory failure who met their inclusion criteria.

According to the acute-on-chronic liver failure (ACLF) definition and diagnostic criteria recently proposed by the Chronic Liver Failure Acute-on-Chronic Liver Failure in Cirrhosis study, ACLF is characterized by acute decompensation of cirrhosis associated with organ/system failure(s) (liver, kidney, brain, coagulation, circulation, and/or lung) and is associated with a short-term (28-day) mortality rate ranging from 23% to 74%, depending on the number of organ failures [5]. A European study reported a 28-day transplant-free mortality in patients with ACLF with 4 organ failures or more of 90% to 100% [6]. Because of the high risk of perioperative mortality, patients with ACLF with multiorgan failure are often considered too sick to undergo a transplant [7].

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However, we believe that if the indication is well-selected in ACLF with multiorgan failure (particularly ARDS), using ECMO as a bridge therapy to deceased donor liver transplant (DDLT) will be a successful choice as in the present case.

## CASE

### History

A 57-year-old female patient was referred to the emergency department because of jaundice and ascites occurring 2 weeks earlier. She had a history of hepatitis B virus infection and was diagnosed with liver cirrhosis 4 years prior but did not take antiviral agents voluntarily. Her initial mental status was drowsy, with an ammonia level of 218  $\mu\text{g/dL}$  and hepatic encephalopathy. Laboratory results revealed a total bilirubin level of 29.1 mg/dL and a Model for End-Stage Liver Disease score of 40 (creatinine, 0.71 mg/dL; international normalized ratio, 6.3).

She was registered with Korean Network for Organ Sharing and waited for DDLT. Fortunately, she was selected as a recipient of DDLT within only 1 day. However, her vital signs became unstable from the day before the operation, and she had hypovolemic shock caused by gastrointestinal bleeding. Thus, inotropics were applied (norepinephrine and vasopressin), and a massive transfusion of fresh frozen plasma and red blood cells was performed.

On the morning of the surgery, her oxygen demand increased up to 9 L of mask oxygen, and bilateral lung haziness was observed on the chest radiograph (Fig 1A). Acute respiratory distress syndrome, transfusion-induced acute lung injury, and pulmonary edema were suspected, and intubation was performed. Because metabolic acidosis, electrolyte imbalance, and pulmonary edema persisted, continuous kidney replacement therapy was applied.

At a fraction of inspired oxygen ( $\text{FiO}_2$ ) of 1.0, the  $\text{PAO}_2$  was measured at 74 mm Hg, the chest radiograph findings worsened because of ARDS, and the demand for inotropics (norepinephrine and vasopressin) increased to the maximum. Four hours before the start of the operation, we applied veno-arteriovenous (VAV) ECMO (Fig 1B).

### Transplant Surgery

The total operation time was 7 hours, and bleeding and coagulopathy were observed during the operation because of heparinization to prevent thrombotic complications within the circuit of ECMO. While stably maintaining an ECMO flow of 4.0 L/min at 2000 to 2200 rpm in the pump setting, the intraoperative vital sign was stably maintained. Additionally, at an  $\text{FiO}_2$  of 0.8 using the ECMO pump, the patient's saturation was well-maintained at 100%. Because of the ECMO line in the vena cava, side-to-side cavocaval anastomosis was performed instead of the conventional technique.

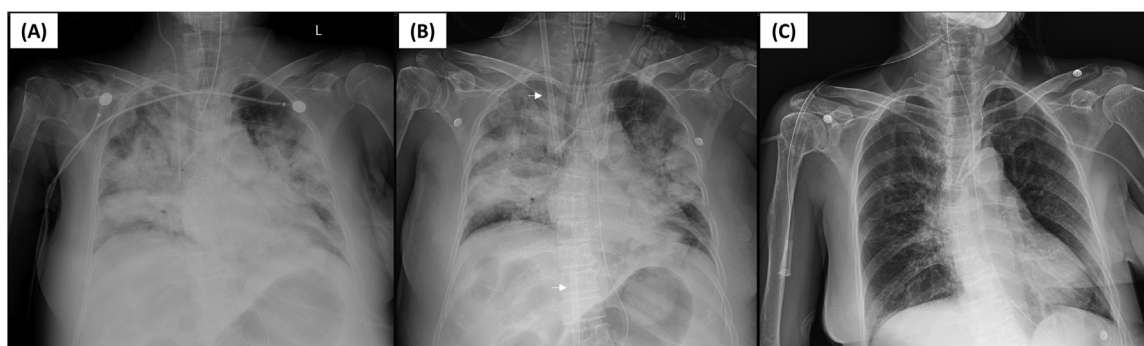
### Postoperative Course

On postoperative days (PODs) 1 and 2, inotropics were tapered, and the ECMO mode was changed from the VAV mode to the venovenous (VV) mode. From POD 3 to 5, as the  $\text{PAO}_2$  of the patient gradually increased, the  $\text{FiO}_2$  of the ventilator and revolutions per minute of VV ECMO were reduced. On POD 6, she was weaned off VV ECMO and decannulated. On POD 7, the chest radiograph findings were improved, and extubation was performed (Fig 1C). She was transferred from the intensive care unit to the general ward on POD 12 (Fig 2).

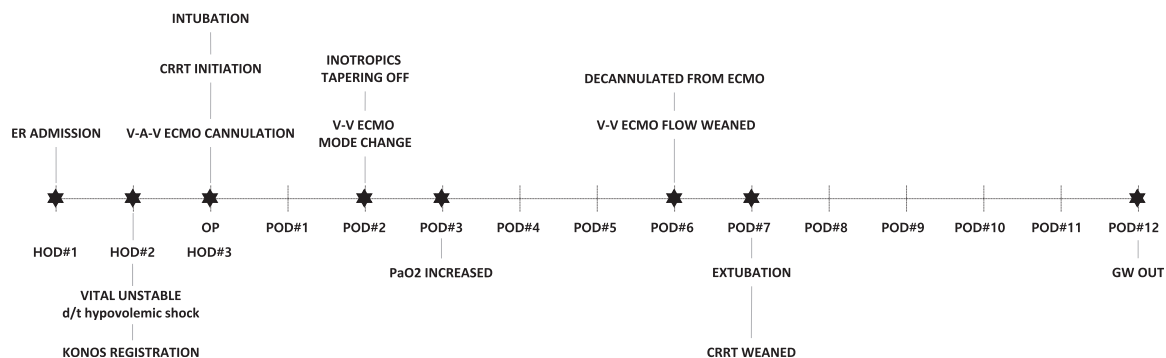
## DISCUSSION

Extracorporeal membrane oxygenation has emerged as an alternative treatment to conventional ventilation maneuvers in the nontransplantation literature to support ARDS. In the case of postoperative respiratory failure and intraoperative cardiac arrest, several case reports have described the successful use of ECMO in the setting of liver transplant (LT) [8–12].

Few case reports have described using ECMO pretransplant or as a bridge to retransplant for patients with reversible multiorgan failure after LT [13,14]. Frank et al described a patient with hepatitis B cirrhosis, hepatocellular carcinoma, and a hypercoagulable state secondary to hepatitis B immunoglobulin administration with initial graft thrombosis and pulmonary embolism that necessitated placement on VV ECMO. Retransplant was successfully performed while receiving VV ECMO



**Fig 1.** Chest radiography of recipient before and after ECMO. **(A)** Chest radiography on the morning of the day of surgery. **(B)** ECMO line cannulated at right jugular vein (arrow), right femoral artery and vein (arrow). **(C)** Chest radiography on postoperative day 8 after weaning off ECMO. ECMO, extracorporeal membrane oxygenation.



**Fig 2.** Summary of clinical course. CKRT, continuous kidney replacement therapy; ECMO, veno-arteriovenous extracorporeal membrane oxygenation; GW, general ward; KONOS, Korean Network for Organ Sharing; POD, postoperative day; VAV, veno-arteriovenous; VV, veno-veno.

[13]. Monsel et al reported a case of a patient with alcohol-related cirrhosis and hepatopulmonary syndrome who presented with acute respiratory failure requiring VV ECMO to maintain oxygenation. The patient progressed to circulatory shock with acute kidney failure and acute liver failure. The patient required VV ECMO for 5 days and then underwent uncomplicated LT on VV ECMO [14].

Because of the high risk of perioperative mortality, patients with ACLF with multiorgan failure are often considered too sick to undergo a transplant and are contraindicated for LT. Moreover, patients with ACLF with respiratory failure ( $PAO_2/FiO_2$  ratio  $<200$ ) are considered contraindicated [7].

However, we showed that in ACLF with multiorgan failure (particularly ARDS), using ECMO as a bridge therapy to DDLT is a successful choice. Because the incidence of severe pulmonary complications resulting in ARDS with multiorgan failure is relatively rare before LT, determining the usefulness of ECMO is challenging. However, in acute but reversible respiratory failure and cardiovascular failure, VAV ECMO provides a useful therapeutic option as a bridge for patients awaiting LT and should be considered if available even with multiorgan failure.

#### DATA AVAILABILITY

Data will be made available on request.

#### DISCLOSURE

All the authors declare no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### REFERENCES

[1] Brodie D, Bacchetta M. Extracorporeal membrane oxygenation for ARDS in adults. *N Engl J Med* 2011;365:1905–14.  
 [2] Definition Task Force ARDS, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA* 2012;307:2526–33.

[3] Sheu CC, Gong MN, Zhai R, Chen F, Bajwa E, Clardy P, et al. Clinical characteristics and outcomes of sepsis-related vs non-sepsis-related ARDS. *Chest* 2010;138:559–67.

[4] Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalanany MM, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. *Lancet* 2009;374:1351–63.

[5] Moreau R, Jalan R, Gines P, Pavesi M, Angeli P, Cordoba J, et al. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. *Gastroenterology* 2013;144:1426–37.

[6] Gustot T, Fernandez J, Garcia E, Morando F, Caraceni P, Alessandria C, et al. Clinical course of acute-on-chronic liver failure syndrome and effects on prognosis. *Hepatology* 2015;62:243–52.

[7] Putignano A, Gustot T. New concepts in acute-on-chronic liver failure: implications for liver transplantation. *Liver Transplant* 2017;23:234–43.

[8] Choi NK, Hwang S, Kim KW, Park GC, Yu YD, Jung SH, et al. Intensive pulmonary support using extracorporeal membrane oxygenation in adult patients undergoing liver transplantation. *Hepatogastroenterol* 2012;59:1189–93.

[9] Yoo CS, Shin YH, Ko JS, Gwak MS, Kim GS. Anesthetic management including extracorporeal membrane oxygenation therapy of liver transplant recipient with life-threatening hypoxemia—a case report. *Korean J Anesthesiol* 2013;65:151.

[10] Tejani M, Yi SY, Eudailey KW, George I, Guarrera JV, Wagnier G. Extracorporeal membrane oxygenation as a rescue device for postreperfusion cardiac arrest during liver transplantation. *Liver Transplant* 2015;21:410–4.

[11] Kim I, Nissen N, Steggerda J, Gereboff A, Sharma V, Kariger R, et al. Venovenous extracorporeal membrane oxygenation for acute respiratory failure in a liver transplant patient: a case report. *Transplant Proc* 2018;50:4038–41.

[12] Van Hoof L, Rega F, Devroe S, Degezelle K, Pirenne J, Neyrinck A, et al. Successful resuscitation after hyperkalemic cardiac arrest during liver transplantation by converting veno-venous bypass to veno-arterial ECMO. *Perfusion* 2021;36:766–8.

[13] Frank PN, Sharma VV, Gereboff A, Guindi M, Kim IK, Kariger R. Hepatitis B immunoglobulin-induced hypercoagulability complicating liver transplantation necessitating ECMO, rescue hepatectomy, and retransplantation. *J Clin Anesth* 2018;44:64–5.

[14] Monsel A, Mal H, Brisson H, Luo R, Eyraud D, Vézinet C, et al. Extracorporeal membrane oxygenation as a bridge to liver transplantation for acute respiratory distress syndrome-induced life-threatening hypoxaemia aggravated by hepatopulmonary syndrome. *Crit Care* 2011;15:1–6.