

The Use of Extracorporeal Circulation in Suspected Brain Dead Organ Donors with Cardiopulmonary Collapse

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Donor shortage is a major limitation in organ transplantation. Several studies have reported that extracorporeal membrane oxygenation (ECMO)-assisted organ donation can be successfully completed without inducing warm ischemia in patients with brain death. The present report described clinical experience of three patients (23-yr old man, 32-yr old man, and 41-yr old woman) who underwent ECMO for the evaluation of brain death and organ donation. They donated six kidneys, three livers, and one both lungs without warm ischemia by ECMO. Six kidney recipients successfully recovered normal status without hemodialysis and two liver recipients survived with normal liver functions, but one liver recipient and one lung recipient died 3 and 15 days after transplantation. Our report strongly encourages ECMO-assisted organ donation from brain death patients with refractory cardiopulmonary collapse to achieve improved organ transplantation.

Keywords: Extracorporeal Membrane Oxygenation; Brain Death; Tissue Organ Procurement

INTRODUCTION

Donor shortage is a major limitation of organ transplantation. According to the data from the Korean Network for Organ Sharing, the prevalence of brain-dead donation in Korea is lower than in other developed countries, as approximately 5.4/1,000,000 person-years (1) and some brain-dead donors fail to complete the donation process because of cardiopulmonary collapse (2). Furthermore, cardiac and/or pulmonary failure have the potential to impair the function of the transplanted organs. In the case of organ failure, extracorporeal membrane oxygenation (ECMO) can rapidly provide excellent cardiopulmonary support that allows organ perfusion without warm ischemia (3-5).

Cardiac arrest or failure are potentially fatal complications which might develop after brain death (6). Fearing this complication, ECMO-assisted organ donation was successfully conducted in brain-dead patients with circulatory failure (7,8). However, the application of ECMO to potentially brain-dead patients with circulatory failure is a controversial ethical issue (9,10). Furthermore, at this time, there is no current guideline for these rare cases.

Recently, the authors performed a successful case of organ donation in a potentially brain-dead patient following cardiac arrest (11). After this experience, the researchers utilized ECMO to diagnose brain death and complete the organ procurement for patients on the verge of brain death with circulatory failure.

The results of this study may help shape clinical guidelines for organ transplantation in potentially brain-dead patients with circulatory collapse.

CASE DESCRIPTION

Case 1

A 23-yr-old man was referred on April 15, 2013 to our center for brain death diagnosis and organ donation after suffering a spontaneous cerebellar hemorrhage. On admission, the Glasgow coma scale (GCS) score was three. Though the initial vital signs were stable with blood pressure (BP) 150/100 mmHg, heart rate (HR) 125/min, and saturation of peripheral oxygen (SpO₂) 100%, BP gradually declined. Transthoracic echocardiogram revealed global hypokinesia with an ejection fraction < 10%. One hour later, his systolic BP decreased to 40 mmHg and remained hypotensive despite medical treatment. Ultimately, cardiac arrest developed and cardiopulmonary resuscitation (CPR) was performed. After 13 min of CPR, venoarterial (VA) ECMO was established. The ECMO flow was set to 4 L/min in order to maintain the mean arterial BP (MAP) above 60 mmHg and SpO₂ 98%. He was diagnosed with brain death by the Brain Death and Organ Donation Committee. After 20 hr of ECMO maintenance, the patient's organs including the liver, both lungs, and both kidneys were successfully retrieved for donation.

Case 2

A 32-yr-old man was diagnosed with acute subarachnoid hemorrhage following a motor vehicle accident. He was referred to our intensive care unit (ICU) from another hospital on November 6, 2013 for the diagnosis of brain death and organ donation. On admission, his BP was 40/18 mmHg, HR 86/min, and SpO₂ 97%. The patient's BP did not respond to dopamine or vasopressin infusions. VA ECMO support was initiated and ECMO flow was set to 5 L/min. The diagnosis of brain death was made by the Brain Death and Organ Donation Committee. After 25 hr of ECMO maintenance, the organs including the liver and both kidneys were successfully retrieved for donation.

Case 3

A 41-yr-old woman was referred to our ICU on April 11, 2014 for the diagnosis of brain death and organ donation. About one month ago, she was found in her house, having hung herself. On admission, the patient's vital signs included BP 112/60 mmHg, HR 114/min, and SpO₂ 100%. One hour after admission, the

patient developed atrial fibrillation with rapid ventricular response and hypotension. Although atrial fibrillation was controlled with amiodarone, hypotension persisted and cardiac arrest developed. VA ECMO was successfully established after 45 min of CPR. The patient was confirmed to be brain dead by the Brain Death and Organ Donation Committee. After 14 hr of ECMO maintenance, the organs including the liver and both kidneys were successfully retrieved for donation.

Outcome after organ transplantation

In total, three patients donated six kidneys, three livers, and one both lungs to six, three, and one patient, respectively (Table 1). The median age of the six patients who underwent kidney transplantation (KT) was 42.5 yr (interquartile range [IQR], 36.3-50.5 yr). Four of these patients were female and they had all been receiving hemodialysis regularly due to end stage renal disease (ESRD). None of the patients experienced primary graft failure or acute rejection after KT. They were discharged without requiring further hemodialysis. During the follow-up period of a

Table 1. Patient clinical features of those who underwent extracorporeal membrane oxygenation for the diagnosis of brain death

No.	Age (yr)	Gender	Cause of brain death	Reason of ECMO	Mode of support	Site of cannulation		Complication	ECMO duration (hr)	Donated organs
						Drain	Perfusion			
1	23	M	Cerebellar hemorrhage	CPR	Venoarterial	Right femoral vein	Left femoral artery	None	20	One both lungs, two kidneys, and liver
2	33	M	Subarachnoid hemorrhage	Refractory circulatory shock	Venoarterial	Left femoral vein	Left femoral vein	None	25	Two kidneys, liver
3	41	F	Hypoxic brain damage	CPR	Venoarterial	Left femoral vein	Left femoral artery	None	14	Two kidneys, liver

CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation.

Table 2. Clinical features of the organ recipients

No.	Age (yr)	Gender	Donor	Donated organ	Reason for organ donation	Acute rejection or primary graft failure	Survival	Lab findings at discharge	Follow-up period, months	Lab findings at last follow-up
1	44	F	Case 1	Left kidney	ESRD	None	Alive	Cr 0.99 eGFR 60.9	19.0	Cr 1.1 eGFR 51.8
2	49	M	Case 1	Liver	Liver cirrhosis	None	Alive	TB 2.7, AST/ALT 357/1,064	17.4	TB 0.6, AST/ALT 24/29
3	59	M	Case 1	Both lungs	RA-ILD	None	Dead due to ventilator-associated pneumonia	-	0.5	-
4	42	F	Case 1	Right kidney	ESRD	None	Alive	Cr 0.9 eGFR 69	18.7	Cr 1.3 eGFR 46.0
5	61	M	Case 2	Liver	Liver cirrhosis	None	Alive	TB 0.7, AST/ALT 9/12	11.6	TB 1.1 AST/ALT 22/22
6	69	M	Case 2	Left kidney	ESRD	None	Alive	Cr 1.71 eGFR 43.0	11.7	Cr 1.0 eGFR 54.7
7	41	M	Case 2	Right kidney	ESRD	None	Alive	Cr 2.65 eGFR 27	10.7	Cr 1.3 eGFR 58.0
8	43	F	Case 3	Right kidney	ESRD	None	Alive	Cr 1.3 eGFR 44.9	6.9	Cr 1.3 eGFR 45.1
9	22	M	Case 3	Left kidney	ESRD	None	Alive	Cr 1.61 eGFR 54.4	6.7	Cr 1.5 eGFR 59.9
10	58	M	Case 3	Liver	Primary malfunction after previous liver transplantation	None	Dead due to multi-organ failure	-	0.1	-

ESRD, end stage renal disease; RA-ILD, rheumatoid arthritis associated interstitial lung disease; Cr, creatinine (mg/dL); eGFR, estimated glomerular filtration rate using the Modification of Diet in Renal Disease Study equation; TB, total bilirubin (mg/dL); AST, aspartate transaminase (IU/L); ALT, alanine transaminase (IU/L).

median of 11.2 months (IQR, 6.9-18.8 months), none of the patients progressed to ESRD requiring hemodialysis.

Two patients with liver cirrhosis due to chronic hepatitis B and one patient with a primary graft failure (after liver transplantation) received liver transplantations. The median age of the three patients who received liver transplantations was 58.0 yr (range, 49-62 yr), and all three were male. During a median of 11.6 (range, 0.1-17.4 months) months of follow-up, two patients had normal liver function. The third patient who had primary graft failure with an earlier liver transplant died 3 days after this transplant due to multi-organ failure.

Two ECMO-supported lung lobes were transplanted to a 59-year-old man who had an acute exacerbation of rheumatoid arthritis associated with interstitial lung disease. He died 15 days after lung transplantation due to hospital acquired pneumonia (Table 2).

DISCUSSION

Organ donation from brain-dead patients has been widely used in many transplantation centers to expand the potential pool of organs. According to a recent report, more than 90% of deceased donors are brain dead (12). However, the relative shortage of organ donation turned the attention to potential donors after circulatory deaths (DCDs). Currently, less than 10% of deceased donations are DCDs (12). Because circulatory deaths develop in many different clinical situations, the Maastricht classification is now widely used to differentiate between different causes (13). Using this system, DCDs are divided into four categories: uncontrolled (type I- brought in dead, type II- unsuccessful resuscitation) and controlled (type III- awaiting cardiac arrest, type IV- cardiac arrest after brain death). If circulatory collapse occurs in potential donors before they are diagnosed with brain death, they cannot be classified as brain-dead donors or as type IV Maastricht patients. In addition, current guidelines do not address this medical complication, and the decision to use these patients for transplantation is controversial.

This study describes the use of ECMO for potentially brain-dead patients with circulatory collapse. In these patients, family members had agreed to organ donation and ECMO application before the final diagnosis of brain death was made. These patients were referred to Samsung Medical Center for brain death evaluations and organ donation. ECMO support was needed to ensure survival while the diagnosis of brain death was made. Two of the patients underwent CPR and VA ECMO support. One patient was placed on ECMO support to manage refractory circulatory shock. In these patients, the use of ECMO helped to successfully maintain adequate organ perfusion. Because ECMO support continued until organ retrieval, there was no warm ischemic time in these patients. Ultimately, 10 major organs including six kidneys, three livers and one both lungs were successful-

ly donated to 10 patients. The outcomes of organ transplantations from these patients were relatively good. Although two patients died, their deaths were not related to the malfunction of the donated organs. During the follow-up period (a median of 11.7 months), no functional decline was seen in the donated organs of the remaining eight patients.

In these cases, EMCO support was initiated immediately before or during the brain death examination. These cases can be controversial because ECMO was used to preserve the functions of potentially useful organs. However, there is no current guideline for this particular clinical situation. As ECMO use becomes more widespread, it is likely that this type of dilemma will be increasingly more common. The authors in one previous article suggested that ECMO support should be considered as a reanimation maneuver during brain death diagnosis (9). The findings of this study suggest that ECMO might be used as an emergent therapy.

Rapid cardiac dysfunction after brain death is a well-known clinical relevance for organ donation (6). According to a study using an animal model of brain death, contractile function was observed to decline by ~50% after 60 min of brain death (14). The most serious event in the heart after brain death is thought to be the loss of the vasculature's sympathetic regulation. This leads to marked vasodilation and intravascular hypovolemia, which results in decreased coronary perfusion pressure and reduction of preload, and therefore decreased contractile function (15). These changes in cardiac function may make brain-dead patients increasingly prone to cardiac arrest.

Before this report, a few studies reported that some patients received ECMO support to permit the end of a brain death diagnosis and organ donations (9,10,16-18). As in our cases, the diagnosis of brain death and organ transplantation were successfully completed in some cases (9,10,18). In contrast, unsuccessful results including failure of brain death diagnosis (10,16) and failure of retrieval of viable organs (17) were also reported. Both successful and unsuccessful cases were also reported (10).

There are three important things that clinicians should consider before using ECMO support to this particular situation. First, although our patients were stable under ECMO support, a few studies reported unsuccessful results as discussed above. Therefore, the diagnosis of brain death needs to be performed more rapidly in patients with hemodynamic deceleration during ECMO support. Second, a decision to apply ECMO support to the suspected brain dead patients with cardiovascular collapse need to be performed very carefully considering that medical resources are limited. Third, there is no current guideline for the apnea test in patients with ECMO support. Therefore, the authors performed apnea test according to a modified protocol developed for this study. Sweep gas flow was adjusted to set pressure of arterial CO₂ (PaCO₂) ranging from 35 to 45 mmHg and mechanical ventilation was changed to T-piece. Sweep gas

flow was then further decreased to 1L/min and 100% of oxygen was delivered through ECMO during the apnea test. The test was considered positive if PaCO₂ increases more than 20 mmHg from the baseline or ≥ 60 mmHg without decrease in PaO₂.

The current guidelines from many institutions including those from the Korean Health Insurance Review and Assessment Service (HIRA) do not approve ECMO for patients with severe neurologic injury and cardiopulmonary instability. However, in this study, the use of ECMO allowed practitioners to complete the diagnosis of brain death and procurement of organs in the 3 patients without warm ischemia. This case and previous reports (9,10) suggest that ECMO support must be considered in such patients, and recognized by the Korean HIRA and other countries' services.

In conclusion, ECMO support can be an option as rescue therapy for the diagnosis of brain death and organ donation in patients with suspected brain death with refractory cardiopulmonary collapse.

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DISCLOSURE

The authors have no potential conflicts of interest to disclose.

AUTHOR CONTRIBUTION

Conception and coordination of the study: Lee H, Cho YH, Sung K. Acquisition of data: Lee H, Cho YH, Sung K, Yang JH, Chung CR, Jeon K, Suh GY. Manuscript preparation: Lee H, Cho YH. Manuscript approval: all authors.

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