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Extracorporeal Life Support in Organ Transplant Donors

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Background: Extracorporeal life support (ECLS) can be applied in brain-dead donors for organ perfusion before donation, thereby expanding the donor pool. The aim of this study was to examine the benefits and early clinical outcomes of ECLS for organ preservation. **Methods:** Between June 2012 and April 2017, 9 patients received ECLS with therapeutic intent or for organ preservation. The following data were collected: demographics, purpose and duration of ECLS, cause of death, dose of vasoactive drugs, and need for temporary dialysis before organ retrieval. The early clinical outcomes of recipients were studied, as well as survival and graft function at 1 month. **Results:** ECLS was initiated for extracorporeal cardiopulmonary resuscitation in 5 patients. The other patients needed ECLS due to hemodynamic deterioration during the assessment of brain death. We successfully retrieved 18 kidneys, 7 livers, and 1 heart from 9 donors. All organs were transplanted and none were discarded. Only 1 case of delayed kidney graft function was noted, and all 26 recipients were discharged without any significant complications. **Conclusion:** The benefits of protecting the vital organs of donors is significant, and ECLS for organ preservation can be widely used in the transplantation field.

Key words: 1. Transplantation
2. Extracorporeal membrane oxygenation
3. Tissue and organ procurement

Introduction

Organ donation and transplant rates vary widely across the world, and the lack of available deceased donors persists. Some desperate patients on long waiting lists even turn to living donors because of the shortage of organs. Organs can only be harvested from deceased donors after the determination of brain death [1]. Severe hypoxic encephalopathy and progression toward brain death are characterized by hemodynamic instability, with a risk of cardiovascular collapse and the possibility that an organ donor may be lost [2]. In several intensive care centers, aggressive organ donor management, including optimal fluid resuscitation and the use of vasopressors, has been described as a strategy to decrease the number of organs lost due to hemodynamic collapse, but some consented organ donors are still lost due to hemodynamic instability [3]. We have used extracorporeal life support (ECLS) to preserve patients' organs for transplantation. In our institution, venovenous ECLS and venoarterial ECLS have become increasingly common modalities of support for patients with reversible cardiac and respiratory failure. Although the outcomes of ECLS have improved, a significant number of patients cannot be weaned from ECLS, either due to irreversible cardiopulmonary dysfunction or neurologic complications.

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Patients with prior overall good health who cannot be weaned from ECLS seem to be prime candidates for organ donation. In this study, we retrospectively analyzed and summarized our experiences and early clinical outcomes of ECLS in donors before organ transplantation.

Methods

Nine donors who received mechanical circulatory support via ECLS for therapeutic purposes or with the intent of organ preservation between June 2012 and April 2017 were included and retrospectively reviewed. Among patients with irreversible ischemic encephalopathy on ECLS, those in whom brain death was not confirmed upon a neurologic assessment, those whose family did not agree to organ donation, and those with multiple organ failure who were not suitable for organ donation as determined by a transplant specialist were excluded from this study, as were hemodynamically unstable brain-dead patients whose family did not want organ-preserving ECLS to be performed.

To make the neurological determination of death, the organ donation unit was involved in evaluating the patients, obtaining family approval, and confirming laboratory data for the determination of brain death. ECLS was implemented as an initial therapeutic tool in 5 patients with severe respiratory or cardiac failure, not for organ preservation. If brain death was confirmed, we used ECLS for its organ-preserving role. During the assessment of brain death, 4 patients needed venoarterial ECLS due to hemodynamic deterioration despite medical intervention after their family member had signed the organ donation consent form. The indications for organ-preservation ECLS included unstable hemodynamics (systolic blood pressure $<$80 mm Hg) with a high dose of vasoactive drugs or a low oxygen saturation (SaO_2 $<$80%) despite ventilatory support with high positive end-expiratory pressure ($>$15 cm H_2O) and a high fraction of inspired oxygen (FiO_2 $>$80%). The femoral artery and vein were cannulated for venoarterial ECLS via the percutaneous approach, and adequate extracorporeal flow was maintained according to each donor's body weight.

The donors were assessed and their suitability for transplantation was evaluated by transplant specialists. At the first assessment, the brain stem reflex had almost disappeared. To check for spontaneous breathing among donors, 95% oxygen was supplied without CO_2 removal via the ECLS oxygenator to the patients for 5 minutes to allow the partial pressure of arterial carbon dioxide ($PaCO_2$) level to rise above 40 mm Hg. Then, the mechanical ventilator was removed and an endotracheal tube was used to supply a FiO_2 of 100% at the rate of 6 L/min. The patient was observed for 10 minutes to check whether spontaneous breathing took place by allowing the $PaCO_2$ level to rise above 60 mm Hg. After confirming the absence of spontaneous breathing, oxygenation with a mechanical ventilator and ECLS were resumed [4].

In all patients on ECLS, the assessment for determining brain death was completed. The following data were collected: demographics, purpose of ECLS, cause of death, duration of ECLS, dose of vasoactive drugs at the initiation of ECLS, and need for temporary dialysis before organ retrieval. The peak values of serum alanine aminotransferase (ALT) and total bilirubin and creatinine levels were analyzed in donors. For patients receiving kidney allografts, delayed graft function was defined as the need for hemodialysis during the first postoperative week. Survival with graft function at 1 month was analyzed. The data were expressed as the median with a range for continuous variables or a percentage of the total number of patients.

Results

We studied 9 organ donors, including 5 women and 4 men who ranged in age from 21 to 63 years (median, 35 years), with severe neurological damage who received ECLS from June 2012 to April 2017. The most common cause of brain death was ischemic encephalopathy after cardiac arrest. In 5 patients, ECLS was initiated as extracorporeal cardiopulmonary resuscitation in response to out-of-hospital cardiac arrest. After the recovery of spontaneous circulation, therapeutic hypothermia was performed. Although cardiopulmonary function was restored, severe hypoxic brain damage developed in these patients. Brain computed tomography scans showed diffuse cerebral edema with effacement of the basal cisterns, suggestive of severe anoxic injury. We obtained consent for organ donation from the patients'

Table 1. Clinical characteristics of donors (n=9)

Characteristic	Value
Age (yr)	35.0 (21–63)
Gender (male/female)	4/5
Blood type (A/B/AB/O)	1/5/1/2
Cause of brain death	
Ischemic encephalopathy after cardiac arrest	4 (44.4)
Cerebral hemorrhage	3 (33.3)
Hypoxic brain damage after hanging	2 (22.2)
Organ-preservation ECLS	4 (44.4)
Duration of ECLS (hr)	47.0 (6.0–135)
Hemodialysis before donation	1 (11.1)
Donation	
Kidney	18
Liver	7
Heart	1

Values are presented as median (range), number, or number (%).
ECLS, extracorporeal life support.

families. The other 4 patients experienced cardiopulmonary failure during an assessment to determine brain death. Transthoracic echocardiography revealed stress-induced cardiomyopathy with severe left ventricular dysfunction in 3 patients, and their median left ventricular ejection fraction (LVEF) was 19.0% (range, 15.0%–25.0%). One patient had refractory hypotension resulting from vasodilatory shock with preserved left ventricular function (LVEF, 65.0%). Thus, we decided to use venoarterial ECLS to complete the assessment in the patients whose condition was severely unstable, requiring them to be sustained with high-FiO_2 mechanical ventilation and a high dose of various vasoactive drugs (Table 1). The peak vasopressor score before the initiation of ECLS was 200 (median, 80.0). The median level of creatinine was 2.82 mg/dL (range, 1.06–5.86 mg/dL) and 1 patient needed hemodialysis before donation. The median total bilirubin level was 1.90 μmol/L (range, 0.70–9.60 μmol/L) and the median ALT level was 290 U/L (range, 76–2,700 U/L) (Table 2). After ECLS, the hepatonephric function of donors significantly improved. We successfully retrieved 18 kidneys, 7 livers, and 1 heart from 9 donors. Their organ retrieval operations were performed at 6.0 to 135.0 hours (median, 80 hours) after being placed on ECLS. All organs were successfully transplanted, and none were discarded. In 1 patient who received a kidney allograft with hemodialysis, delayed graft function was observed, and all 26 recipients were discharged after healing.

Table 2. Vasopressor scores and laboratory indicators of donors (n=9)

Variable	Median (range)
Vasopressor score[a)]	80.0 (0–200.0)
Alanine aminotransferase (U/L)	290 (76–2700)
Total bilirubin (μmol/L)	1.9 (0.7–9.6)
Creatinine (mg/dL)	2.82 (1.06–5.86)

[a)](Dopamine [μg/kg/min]×1)+(dobutamine [μg/kg/min]×1)+(epinephrine [μg/kg/min]×100)+(norepinephrine [μg/kg/min]×100).

Discussion

Organ transplantation faces the challenge of an ongoing organ shortage. To increase the organ pool, some strategies have been developed for the management of brain-dead patients, who remain the primary source of organs for transplant [4].

ECLS is a useful treatment for refractory cardiac or respiratory failure. Implementing ECLS in cardiac arrest patients can rapidly stabilize their circulation, and ECLS has been used to assist in cardiopulmonary resuscitation [5]. However, ECLS in patients undergoing cardiopulmonary resuscitation can take longer and there is a higher risk of procedural failure and complications. A long interval between cardiac arrest and initiation of extracorporeal circulation may be tolerated by major organs except the brain, which is the most sensitive to hypoxia. Thus, poor neurological outcomes despite preserved function of vital organs other than the brain can result from extracorporeal cardiopulmonary resuscitation [6]. These patients can be potential organ donors, after consent is obtained from their families. A retrospective study between 1995 and 2012 identified 41 organ donors who had been previously supported by extracorporeal circulation for therapeutic purposes. Kidney graft function was satisfactory compared with donors on non-ECLS, but there was a higher discard rate of liver grafts [7].

Intracranial hypertension after brain stem infarction causes the loss of blood pressure autoregulation and sympathetic tone, with a reduction in systemic vascular resistance and vasodilatation. Thus, some consented organ donors are lost due to hemodynamic instability, even with optimal organ donor management through mechanical ventilation and various vasoactive drugs, and high-dose β-agonists may result in detrimental vasoconstriction in donor or-

gans [8]. The dose of vasoactive drugs needed to maintain adequate perfusion was reduced after the implementation of ECLS in this study. We used ECLS for potential donors with hemodynamic instability to prevent the failure of medical support. The timing of ECLS remains an unresolved issue. We considered that the potential donor needed ECLS when maximal medical support did not allow the procedures for assessing brain death and preserving visceral organs to be performed. Because there was no definitive guideline for management of patients on ECLS during brain death assessment, we tried to maintain the mean arterial pressure >80 mm Hg and SaO_2 >95% with a minimal dose of a vasopressor and FiO_2 from a mechanical ventilator. Transportation to the operating room and organ retrieval were performed under ECLS. We did not find any published guidelines concerning the implementation of ECLS for organ preservation. As with the process of organ donation from a brain-dead patient, organ-preservation ECLS has both potential benefits and risks. ECLS is invasive and can damage the physical integrity of a brain-dead patient. In addition, organ-preservation ECLS may have the risk of psychological harm to the family members and clinicians due to its invasiveness, and it can cause confusion, since ECLS is usually used as a life-saving intervention. The application of organ-preservation ECLS before the declaration of brain death has been described in some case reports, but it poses some problems [9,10]. ECLS requires anticoagulation, and it has the potential risk of intracranial hemorrhage and can hasten death [11]. In severely brain-injured patients, the evolution of brain death is difficult to predict and the implementation of organ-preservation ECLS in these patients has no benefit if brain death has not occurred. These patients may have brain activity and can suffer [12].

In our study, transplanted renal allografts procured from donors on ECLS were successfully transplanted, and none were discarded. These results were similar to what was expected from donors on non-ECLS, with favorable graft survival. All liver allografts survived with no incidence of primary non-function. The heart of a donor who had received 2 hours of cardiopulmonary resuscitation before implementation of ECLS was retrieved and successfully transplanted without early graft dysfunction.

Our study has some limitations. The clinical data used in this study represent a retrospective review of a small population of organ donors and recipients. Follow-up data were obtained over a short period and were limited, as the recipients were followed up at multiple institutions. Currently, the application of ECLS in brain-dead donors is still in the clinical exploration stage and there are some ethical controversies [13], but the effects on protecting vital organs of donors are significant and organ-preservation ECLS can be widely used for transplantation with improvements in perfusion technology.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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