Received: 1 June 2023 | Revised: 17 August 2023 | Accepted: 29 September 2023

DOI: 10.1002/ags3.12749

AGSurg Annals of Gastroenterological Surgery Open Access WILEY

ORIGINAL ARTICLE

Using extracorporeal membrane oxygenation in donations after cardiac death or brain death: A single-center experience and long-term outcome

Chia-En Hsieh[1] | Ya-Lan Hsu[1] | Yao-Li Chen[2,3] | Hsin-Rou Liang[4] | Kuo-Hua Lin[5] | Wen-Yuan Chen[6] | Hsiu-Man Wu[7] | Sin-Bao Hunang[8,9] | Yu-Ju Hung[2]

[1]Department of Nursing, Liver Transplantation Center, Chung Shan Medical University Hospital, Taichung, Taiwan

[2]Department of Surgery, Liver Transplantation Center, Chung Shan Medical University Hospital, Taichung, Taiwan

[3]School of Medicine, Chung Shan Medical University, Taichung, Taiwan

[4]Department of Surgery, Kaohsiung Medical University Chung-Ho Memorial Hospital, Kaohsiung, Taiwan

[5]General Surgery, Changhua Christian Hospital, Changhua, Taiwan

[6]Department of Pharmacy, Liver Transplantation Center, Chung Shan Medical University Hospital, Taichung, Taiwan

[7]Department of Nursing, Changhua Christian Hospital, Changhua, Taiwan

[8]Department of Family and Community Medicine, Chung Shan Medical University Hospital, Taichung, Taiwan

[9]Department of Medical Humanities, School of Medicine, Chung Shan Medical University, Taichung, Taiwan

Correspondence
Yu-Ju Hung, Department of Surgery, Liver Transplantation Center, Chung Shan Medical University Hospital, Taichung, Taiwan.
Email: yuju149116@gmail.com

Abstract

Aims: The use of extended criteria donors is a routine practice that sometimes involves extracorporeal membrane oxygenation (ECMO) in donations after cardiac death or brain death.

Methods: We performed a retrospective study in a single center from January 2006 to December 2019. The study included 90 deceased donor liver transplants. The patients were divided into three groups: the donation after brain death (DBD) group ($n=58$, 64.4%), the DBD with ECMO group ($n=11$, 12.2%) and the donation after cardiac death (DCD) with ECMO group ($n=21$, 23.3%).

Results: There were no significant differences between the DBD with ECMO group and the DBD group. When comparing the DCD with ECMO group and the DBD group, there were statistically significant differences for total warm ischemia time ($p<0.001$), total cold ischemia time ($p=0.023$), and split liver transplantation ($p<0.001$), and there was significantly poor recovery in regard to total bilirubin level ($p=0.027$) for the DCD with ECMO group by repeated measures ANOVA. The 5-year survival rates of the DBD, DBD with ECMO, and DCD with ECMO groups were 78.1%, 90.9%, and 75.6%, respectively. The survival rate was not significantly different when comparing the DBD group to either the DBD with ECMO group ($p=0.435$) or the DCD with ECMO group ($p=0.310$).

Conclusions: Using ECMO in donations after cardiac death or brain death is a good technology, and it contributed to 35.6% of the liver graft pool.

KEYWORDS
donation after brain death, donation after cardiac death, extracorporeal membrane oxygenation, liver transplantation, long-term outcome

1 | INTRODUCTION

According to the Taiwan Organ Registry and Sharing Center, there were 15.2 donors per million deaths in 2019. However, after excluding single tissue donation, the number of organ donors was only 5.6 per million deaths in 2019. End-stage liver or renal disease patients on long waiting lists turn to living organ donors. Facing the shortage of available organs, the Taiwan Organ Registry and Sharing Center has promoted "controlled donation after cardiac death" in recent years. Donations after cardiac death or donation after circulatory death numbers were more than 10%–20% of all deceased donors.[1,2] Controlled donation after cardiac death (DCD) had the major issue of warm ischemic time, and reported to have significantly more substantial ischemic injury (high peak alanine aminotransferase and biliary strictures), and increased the risk of delayed graft function, graft loss, and mortality.[3,4] Our institution had started the process for donation after brain death (DBD) with extracorporeal membrane oxygenation (ECMO) during the brain-death determination in 2008,[5] and utilized ECMO to provide hypothermic perfusion in controlled DCD since 2014. Using the extended criteria in organ donations is an approved strategy to increase the pool of organs, and ECMO can be used after cardiac death or brain death. We presented the short-term and long-term outcomes of liver transplants involving DBD with ECMO or DBD with ECMO.

2 | MATERIALS/PATIENTS AND METHODS

This retrospective review describes patients with ECMO support in brain death and cardiac death. Donations of liver grafts from such patients have the potential to increase the applicability of transplantation as a treatment for end-stage organ disease. We introduced the work of the Organ Donation Crew of Changhua Christian Hospital between January 2006 and December 2019 (94 liver transplantations). The grafts from DCD without ECMO support ($n=2$) and deaths occurring ≤72 h after transplantation ($n=2$, bleeding) were excluded. There were 90 liver transplantations (LT) included. The patients were divided into three groups: the DBD group ($n=58$, 64.4%), the DBD with ECMO group ($n=11$, 12.2%) and the DCD with ECMO group ($n=21$, 23.3%). The study was approved by the Institutional Review Board of the Changhua Christian Hospital (No. CCH 191244).

2.1 | Donation after brain death (DBD) with ECMO

The donors had either (1) systolic blood pressure below 90 mm Hg after resuscitation and under two vasopressor agents using or (2) low oxygen saturation (SaO_2 90%) under mechanical ventilation with high-level positive end-expiratory pressure and high demand of oxygen ($FiO_2 \geq 80\%$) were indicated for ECMO support during the brain-death determination after obtaining the consent from the donor's family.[5] After assessment of brain death twice (Figure 1), liver graft was harvested and implanted as a treatment for end-stage liver disease.

2.2 | Donation after cardiac death (DCD) with ECMO

Controlled DCD (Maastricht type III donors) typically involves a mechanically ventilated patient with overwhelming single or two organ failure, usually involving a severe brain injury ($n=20$) or myocardial infarction combined with hypoxia encephalopathy ($n=1$).[6] With the family's agreement, a decision is made to withdraw life-sustaining treatment.

Parameters were as follows: mean arterial pressure ≤ 50 mm Hg. Functional warm ischemia time (WIT) was defined as the period from the occurrence of any hemodynamic parameters until the start of in situ cold perfusion. After declaring cardiac death (5 min of cardiac standstill), rapid cooling by ECMO preservation methods achieved the core temperature around 10–20°C (Figure 1). The unique ability of ECMO to provide hypothermic perfusion and reduce WIT. Organ procurement would follow by the ECMO setup. Once the moderately rapid infusion of cold preservation solution (HTK solution) into the portal and aortic cannulation, the ECMO would be stopped and started as cold ischemia time (CIT) period.

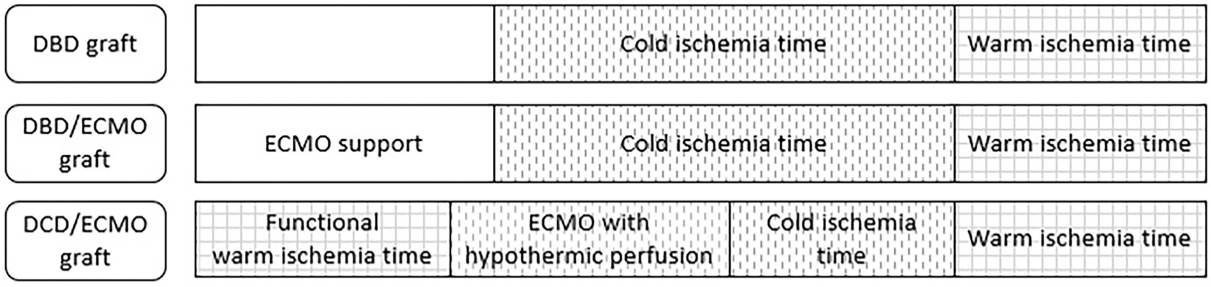

FIGURE 1 Processes for extended criteria liver donation. The process of donation after brain death (DBD) included brain-death determination, cold ischemia time and warm ischemia time. The process of DBD with extracorporeal membrane oxygenation (ECMO) included brain-death determination during ECMO, cold ischemia time, and warm ischemia time. The process of donation after cardiac death (DCD) with ECMO included functional warm ischemia time after withdrawing life-sustaining treatment, cooling perfusion by ECMO after cardiac death was declared, cold ischemia time, and warm ischemia time.

2.3 | Definitions

CIT (minutes) is indicated as the period from aortic clamping and infusion of cold preservation solution (HTK solution) in the graft until putting the graft into the recipient's abdominal cavity. WIT is defined as the time interval from placing the graft into the abdominal cavity until detaching the vascular clamps after finishing all venous anastomoses (IVC piggy-back or hepatic vein and portal vein anastomoses). Total WIT is defined as functional warm ischemic time plus WIT. In the DCD with ECMO group, total CIT is defined as the time taken for ECMO to provide hypothermic perfusion plus the CIT (Figure 1).

2.4 | Statistical analysis

We had correlated clinical factors, including age, model for end-stage liver disease (MELD) score, blood loss, CIT, WIT, ECMO with hypothermic perfusion, functional WIT, international normalized ratio (INR), alanine aminotransferase (ALT), total bilirubin, gamma-glutamyl transferase (GGT), length of stay, post LT complications, and hospital mortality. All data were recorded on a computerized database. The patients were classified into three groups: DBD, DBD with ECMO, and DCD with ECMO. Pearson's chi-squared test, Fisher's exact test, *t*-tests for independence, the Mann–Whitney test, and repeated measures ANOVA were used to examine differences in the demographic factors and the clinical characteristics of the patients. Values for the continuous variables are presented as mean ± standard deviation (SD) in this study. A p value less than 0.05 was considered to be statistically significant. All statistical analysis was performed with SPSS (Statistical Package for Social Science, version 20.0).

3 | RESULTS

Ninety LT patients were included in this study. There was not any significant difference in demographic data and clinical features between the DBD with ECMO group and the DBD group. There were statistically significant differences between the DCD with ECMO group and the DBD group in items of total WIT ($p<0.001$), total CIT ($p=0.023$) and proportion of split LT ($p<0.001$) (Table 1). In the DCD with ECMO group, the ECMO with hypothermic perfusion time (mean ± standard deviation) was 76.81 ± 20.38 min (range 34.00–126.00), and the functional WIT was 22.48 ± 17.07 min (range 6.00–68.00). Six patients had the functional WIT above 30 min. The most common causes of hospital death were infection ($n=4$) and graft-versus-host disease ($n=1$, DCD with ECMO group). There were no patients who developed any ischemic-type biliary stricture complications after LT, but one patient in the DCD with ECMO group had repeated cholangitis that was treated with antibiotics.

The DBD with ECMO group had significantly higher INR level than the DBD group ($p=0.048$) on postoperative day 7. However, the DCD with ECMO group had significantly lower INR level than the DBD group ($p=0.030$) on postoperative day 1. INR level showed significantly different time points for DBD with ECMO versus DBD ($p<0.001$) and for DCD with ECMO versus DBD ($p<0.001$) by repeated measures ANOVA. Over various postoperative days, ALT levels showed no significantly difference when comparing both the DBD with ECMO group and the DCD with ECMO to the DBD group. ALT level showed significantly different time points for DBD with ECMO versus DBD ($p=0.006$) and for DCD with ECMO versus DBD ($p<0.001$) by repeated measures ANOVA. In the DBD with ECMO group and the DCD with ECMO group, total bilirubin level was not significantly different compared to the DBD group over various postoperative days. Total bilirubin level showed significantly different time points for DBD with ECMO versus DBD ($p=0.027$) and for DCD with ECMO versus DBD ($p=0.001$), and it had significantly different time × group for DCD with ECMO versus DBD ($p=0.027$) by repeated measures ANOVA. Over various postoperative days, GGT level was not significantly different when comparing both the DBD with ECMO group and the DCD with ECMO group to the DBD group. GGT level showed significantly different time points for DBD with ECMO versus DBD ($p<0.001$) and for DCD with ECMO versus DBD ($p<0.001$) by repeated measures ANOVA (Figure 2).

The 1-year survival rate of the DBD, DBD with ECMO, and DCD with ECMO groups were 94.8%, 90.9%, and 75.6%, respectively. The 5-year survival rates of the DBD, DBD with ECMO, and DCD with ECMO groups were 78.1%, 90.9%, and 75.6%, respectively. When compared to the DBD group, the DBD with ECMO group ($p=0.435$) and the DCD with ECMO group ($p=0.310$) did not have significantly different survival rates (Figure 3). The causes of death in DBD group included cancer ($n=7$, hepatocellular carcinoma recurrent = 5, esophageal cancer = 1, cholangiocarcinoma metastatic = 1), acute hepatitis B infection with acute hepatic failure = 1, sepsis = 1, chronic graft rejection = 1, and sudden cardiac death = 1. In DCD with ECMO group, causes of hospital death included pancreas cancer = 1 and sepsis = 2.

4 | DISCUSSION

Severe head injury combined with cardiac or respiratory failure posed a challenge in performing apnea testing during brain-death determination in patients with ECMO. ECMO is a technique used in the most hemodynamically unstable patients who are treated with two vasopressor agents, and also in respiratory failure patients with refractory hypoxia (e.g., severe hemopneumothorax, pulmonary edema or acute respiratory distress syndrome) during the brain-death determination. Veno-arterial extracorporeal membrane oxygenation (V-A ECMO) has the advantage of providing complete cardiac and respiratory support. To be clinically evaluated, a patient must show evidence of cerebral unreceptivity and un-responsivity with absence of brainstem reflexes. To performing apnea test with ongoing V-A ECMO or with an oxygenator with ECMO, set the FiO_2 to 100% for 10 min before ventilator disconnection. ECMO can easily

TABLE 1 Comparisons of demographic data and clinical features of three groups of liver transplantation patients.

	DBD	DBD/ECMO	DCD/ECMO	DBD vs. DBD/ECMO	DBD vs. DCD/ECMO
	n = 58	*n* = 11	*n* = 21		
Demographic and clinical features	**Mean ± SD (range)**	**Mean ± SD (range)**	**Mean ± SD (range)**	***p***	***p***
Recipient age (years)	49.59 ± 9.71 (34–70)	52.55 ± 7.92 (41–64)	52.86 ± 9.13 (35–65)	0.290	0.334
Donor age (years)	39.43 ± 15.49 (12–79)	42.73 ± 14.91 (17–65)	46.00 ± 16.43 (19–70)	0.497	0.092
MELD score	17.76 ± 8.00 (7.0–40.0)	18.00 ± 6.03 (8.0–30.0)	15.62 ± 5.77 (7.0–28.0)	0.730	0.414
Blood loss (mL)	3321.55 ± 2898.56 (300.0–14 800.0)	2190.91 ± 1220.82 (800.0–5000.0)	2930.95 ± 2405.18 (200.0–9000.0)	0.286	0.706
Function WIT (min)			22.48 ± 17.07 (6.00–68.00)		
ECMO with hypothermic perfusion (min)			76.81 ± 20.38 (34.00–126.00)		
Total WIT (min)	19.22 ± 7.96 (7.00–47.00)	19.36 ± 6.05 (12.00–32.00)	40.57 ± 18.08 (18.00–78.00)	0.928	<0.001
Total CIT (min)	153.16 ± 108.88 (25.0–505.0)	137.45 ± 75.75 (37.0–292.0)	185.43 ± 62.62 (117.0–357.0)	0.922	0.023
Length of stay (days)	23.62 ± 9.92 (11.00–62.00)	34.27 ± 22.97 (13.00–85.00)	30.95 ± 17.90 (15.0–69.00)	0.189	0.259
	(%)	**(%)**	**(%)**		
Vasopressors in donor					
No	14 (24.1)	0 (0.0)	7 (33.3)	0.104	0.414
Yes	44 (75.9)	11 (100.0)	14 (66.7)		
Split liver transplant					
No	33 (56.9)	7 (63.6)	21 (100.0)	0.750	<0.001
Yes	25 (43.1)	4 (36.4)	0 (0.0)		
Rejection					
No	56 (96.6)	9 (81.8)	18 (85.7)	0.117	0.114
Yes	2 (3.4)	2 (18.2)	3 (14.3)		
Delayed graft function					
No	54 (93.1)	10 (90.9)	19 (90.5)	1.000	0.654
Yes	4 (6.9)	1 (9.1)	2 (9.5)		
Hospital mortality					
No	56 (96.6)	10 (90.9)	19 (90.5)	0.411	0.286
Yes	2 (3.4)	1 (9.1)	2 (9.5)		
Repeated cholangitis					
No	58 (100.0)	11 (100.0)	20 (95.2)	–	0.266
Yes	0 (0.00)	0 (0.0)	1 (4.8)		

Abbreviations: CIT, cold ischemia time; MELD, Model for End-Stage Liver Disease score; WIT, warm ischemia time.

provide high blood oxygen levels in organs than ventilator. When the ventilator disconnected, oxygenator air flow of ECMO was also closed. A targeted mean blood pressure of more than 60–70 mm Hg is recommended when setting the pump speed. Besides, ECMO can decrease the risk of cardiac arrest in the respiratory acidosis phase, which might lead to shock, hypoxia, or coronary artery low profusion. Once the brain-death determination finished (if success or failure), oxygenator air flow of ECMO was rapidly increased to wash out carbon dioxide, keep blood oxygenation, and decrease respiratory acidosis.

The apnea test is employed to assess respiratory drive when the arterial partial pressure of carbon dioxide rises beyond the apneic threshold, which will stimulate the medullary respiratory center. The absence of respiratory effort or movement when $PaCO_2$ exceeds 60 mm Hg is indicative of brain death. In patients with ECMO support, to reach the apneic threshold, either lower the air gas flow rate to reduce carbon dioxide elimination, or add exogenous carbon dioxide to the gas blender at the extracorporeal circuit to achieve hypercapnia is needed.[7] However, once the oxygenator has higher air flow, carbon dioxide will be washed out (arterial $PaCO_2 < 60$ mm Hg), and the addition of exogenous carbon dioxide might result in respiratory acidosis. In our practice, when oxygenator air flow of ECMO reduced, we adjusted the pump speed and used vasopressor agents to keep the mean blood pressure above 60 mm Hg. It is a valid method for conducting apnea tests with ECMO support, two donors failed the brain-death determination exam in the study period. Apnea testing is an essential component in the clinical determination of brain death. Under physiological apnea states, the $PaCO_2$ level is predicted to increase by 3–4 mm Hg/min in such situations.[8] The main purpose of apnea test is to allow increasing serum carbon dioxide level in central nervous system, which would normally stimulate the respiratory centers in a functioning medulla. On the other hand, donors with no medullary function will not make any spontaneous respiratory effort in the setting of profound hypercarbia and acidosis.[9] The negative test of outcome is defined by any spontaneous respiratory efforts in response to hypercapnic and acidotic stimulation; the positive test is the absence of any respiratory activity under this condition. The two donors appeared to have spontaneous respiratory efforts (negative test of outcome) during their apnea tests.

Hemodynamic instability and poor oxygenation, marginal grafts, and using the ex vivo technique were considered as contraindications to splitting liver transplantation.[10] ECMO is a rapidly mechanical assist device for supporting the circulatory and respiratory systems. When hemodynamic failure to recover and can prevent organ damage from hypoperfusion, using ECMO improves organ perfusion, increased partial pressure of arterial oxygen, and decreased lactic acid level. This technique allows reduction of the need for inotropes or vasopressors. The use of DBD with ECMO group (whole liver transplantation $n = 7$, split liver transplantation $n = 4$) is considered similar to that of DBD group in terms of postoperative graft function, primary nonfunction, and complications in this study. The two split donors were 35 and 42 years old. WIT were 16 and 18 min and CIT were 37 and 76 min in right lobe liver transplantation, WIT were 15 and 15 min and CIT were 139 and 194 min in left lobe liver transplantation. The in situ procedure was chosen for the following reasons: (1) both donors were hemodynamic stable on ECMO, (2) very short graft ischemia times, (3) it provides superior and young grafts, and (4) split right lobe using living liver donor technique, (5) split left lobe (with middle hepatic vein) was piggyback technique in orthotopic liver transplantation. We propose that using DBD with ECMO should not be considered as a contraindication to splitting liver transplantation, that was also similar to the method in one study.[11] This technique (DBD with ECMO, $n = 11$) was applied 15.9% of DBD donors (DBD with/without ECMO donors $n = 69$).

From the declaration of cardiac death (5 minutes after a flat electrocardiogram) to the completion of organ procurement, the warm ischemic time (WIT) of liver may extend beyond 60 minutes. ECMO can provide hypothermic perfusion by rapid cooling to 10–20°C and reduce WIT time in DCD for transferring donor to operative room and operative to arterial cannulation time. There are two other benefits of using ECMO in DCD donors in clinical practice. First, the cardiac death determination can take place in intensive care unit, instead of occupying the operating room, especially fail (alive) or WIT over 120 min. Second, there are much enough time for transferring donor to operative room and the organ procurement procedure.

Patients in the DCD group or DBD with ECMO group showed significantly poor recovery of bilirubin levels compared to the DBD group. WIT was longer in DCD with ECMO group. Once unstable hemodynamic (high dose or two vasopressor agents) and low oxygen saturation happened to DBD donor, the grafts might become hypoperfusion and marginal graft. Using ECMO improved organ perfusion and maintain oxygen saturation during brain-death determination. In the short term, DBD with ECMO group showed poor recovery of bilirubin and INR levels than DBD group. Hepatic ischemia reperfusion injury developed cellular metabolic disturbances, lack of oxygen supply and ATP depletion, and profound inflammatory immune response that involves both direct and indirect cytotoxic mechanisms, the risk of early and late graft dysfunction of donor livers is directly related to hepatic ischemia reperfusion injury.[12,13] In situ normothermic machine perfusion circuit significantly reduced complications related to ischemia–reperfusion injury compared to a conventional approach, and granting a consistent reduction of graft complications.[14] Normothermic ECMO perfusion can re-establish circulation to some parts of the body, however, the use of normothermic perfusion in this context remains ethically controversial.

There was no significant difference between the DBD group and the DBD with ECMO group regarding recipient survival. Bronchard et al.[15] reported a similar result. In the selection of splitting liver graft, many reports recommended the following criteria: hemodynamically stable, younger donors (below aged of 40–55), less than 30% hepatic steatosis, ALT <60 U/L, Na < 160 mmol/L, duration of intensive care unit treatment less than 5 days, single vasopressor and low inotropic support.[16] Assalino et al.[11] also reported two DBD

donors underwent in situ liver splitting transplantation with ECMO support. We have performed four DBD with ECMO LT involving situ liver splitting. One recipient had hospital mortality due to sepsis, and the other recipients survived over 5 years ($n=1$) or between 3 and 5 years ($n=2$).

To face the organ shortage, the Taiwan Organ Registry and Sharing Center has promoted "controlled donation after cardiac death." After cardiac-death declaration (5 min of cardiac standstill), ECMO can be used along with hypothermic perfusion in an abdominal organ (liver or kidney). We used ECMO technology to improve

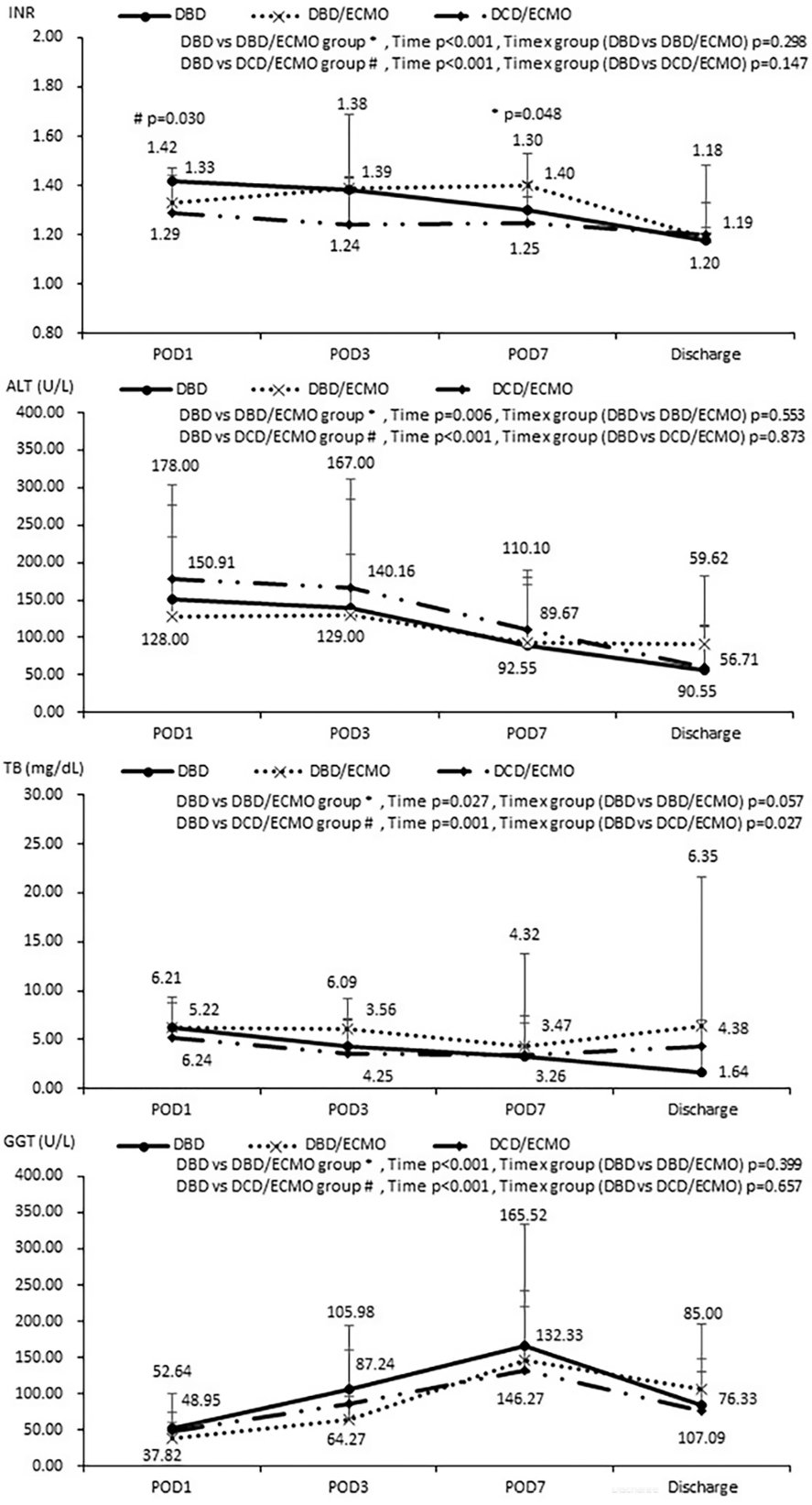

FIGURE 2 Liver function comparisons among three groups were assessed for postoperative days 1, 3, and 7 and day of discharge by repeated measures ANOVA. International normalized ratio (INR) level showed significantly different time when comparing the donation after brain death (DBD) group to the DBD with extracorporeal membrane oxygenation (ECMO) group ($p < 0.001$) and the donation after cardiac death (DCD) with ECMO group ($p < 0.001$). Alanine aminotransferase (ALT, U/L) level showed significantly different time for DBD with ECMO versus DBD ($p = 0.006$) and for DCD with ECMO versus DBD ($p < 0.001$). Total bilirubin (TB, mg/dL) level showed significantly different time for DBD with ECMO versus DBD ($p = 0.027$) and for DCD with ECMO versus DBD ($p = 0.001$), and it had significantly different time × group for DCD with ECMO versus DBD ($p = 0.027$). Gamma-glutamyl transferase (GGT, U/L) level showed significantly different time for DBD with ECMO versus DBD ($p < 0.001$) and for DCD with ECMO versus DBD ($p < 0.001$).

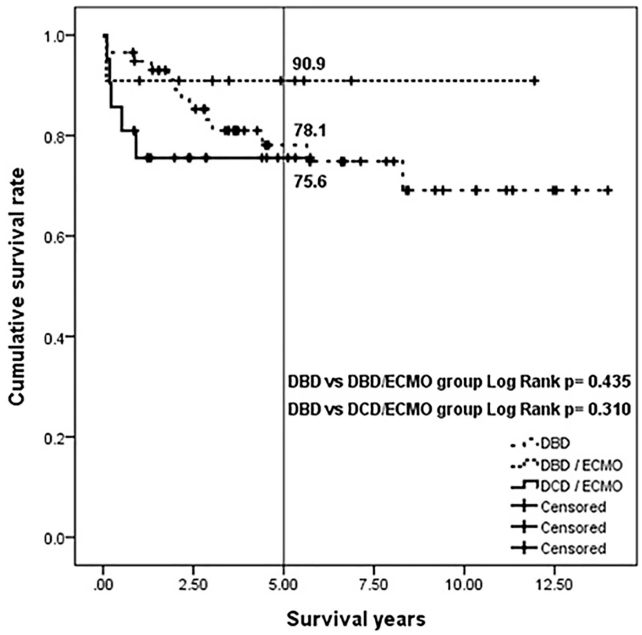

FIGURE 3 Five-year patient survival rates for three groups. The 5-year patient survival rates of the donation after brain death (DBD), DBD with extracorporeal membrane oxygenation (ECMO), donation after cardiac death (DCD) with ECMO groups were 78.1%, 90.9%, and 75.6%, respectively. The patient survival rates for the DBD with ECMO group ($p = 0.435$) and the DCD with ECMO group ($p = 0.310$) were not significantly different from the patient survival rate of the DBD group.

the outcome of DCD LT by restoring the circulation of oxygenated blood to the abdominal organs in the donor. Functional WIT was 22.48 ± 17.07 min (range 6.00–68.00). The time for ECMO with hypothermic perfusion was 76.81 ± 20.38 min (range 34.00–126.00). The DCD with ECMO group had significantly longer total WIT ($p < 0.001$) and total CIT ($p = 0.023$) than the DBD group. Six patients had over 30 min of functional WIT (44.5 ± 14.40 min, range 34–68 min, median 36.5 min). One patient died from graft-versus-host-disease in the hospital, and the other five patients were alive at the time of writing. During the follow-up period, there was no ischemic-type biliary stricture complication after LT. We believed that functional WIT could be safely extended to 40 min, however sample size was relatively small; Mihaylov et al.[17] suggested extended to 40 min as well. The WIT in DCD with ECMO group was twice as long as the DBD group and the DBD with ECMO group. In the DCD with ECMO group, there was poor recovery of the short-term total bilirubin level ($p = 0.027$) by repeated measures ANOVA; therefore, split LT is not recommended.

Delayed graft function occurred for four split grafts (one hospital death in DBD group), one marginal graft (severe hepatic steatosis), and two DCD with ECMO grafts. The use of ECMO in supporting circulatory and respiratory functions during DBD can reduce liver injury from vasoactive drugs, and the primary non-function of the liver graft was reported to be zero.[18] In our study, ECMO kept the graft perfusion quality and reduced the graft discard rate. Hospital deaths were caused by infection ($n = 4$, three split grafts and one DCD with ECMO graft) and graft-versus-host disease ($n = 1$, DCD with ECMO group). We found that the 5-years survival rate in DBD group was similar with the DBD with ECMO group ($p = 0.435$) and the DCD with ECMO group ($p = 0.310$). The other review article indicated that the 1-year DCD patient survival rate was 74%–84%, and DCD liver grafts remain at increased risk of postoperative biliary complications, especially ischemic cholangiopathy.[19] A recent European study found that the 1-year survival rate for 1497 recipients receiving controlled DCD was 90%.[20] However, in our study the 1-year survival rate was 75.6% ($n = 2$ in hospital mortality, $n = 2$ due to sepsis shock related to intra-abdominal infection, $n = 1$ due to recurrent hepatocellular carcinoma) and 90.9% ($n = 1$ in hospital mortality), respectively, for the DCD with ECMO group and the DBD with ECMO group. Ischemic-type biliary stricture complications can occur after LT due to prolonged cold-warm ischemic time or shock liver, but there were none in this study.

The liver machine perfusion techniques can be divided into two major subtypes, including normothermic machine perfusion and the other machine perfusion (sub-normothermic machine perfusion or hypothermic machine perfusion). Sub-normothermic machine perfusion and hypothermic machine perfusion of the liver needs a no red blood cell solution containing oxygen. Hypothermic machine perfusion could protect against initiation ischemic reperfusion injury, oxygenation of the perfusate during hypothermic oxygenated perfusion leads to metabolic resuscitation with resynthesis of adenosine triphosphate and cellular energy charge during cold perfusion, the biliary tree is protected from the injury and complications after LT.[21,22] Normothermic machine perfusion has been used recently in graft preservation, especially in DCD or extended donation criteria. Normothermic machine perfusion can restore and maintain liver function at body temperature, to assess liver function and predict the quality of the donor organ by the bile production, metabolic and dynamic parameters.[23] The material cost of machine perfusion is too expensive, especially in small organ donation centers. Extracorporeal support with oxygenation in DCD has been reported to increase the available number

of donors by approximately 33%, ECMO facilities should embed local programs for donation after cardiac-death in the emergency department or intensive care.[24]

According to the Taiwan Organ Registry and Sharing Center, there were 118 liver grafts from deceased donors in 2019 (DCD grafts: $n=7$, DBD grafts: $n=111$). In recent years, donation after circulatory death has received increased attention worldwide. Since the success of DCD LT depends on preservation methods to maintain viability, many machine perfusion systems were developed. However, ex situ liver machine perfusion is complicated and expensive, comparing to ECMO, which is easier and cheaper. Our study had certain limitations. First, the study was retrospective, and the data were collected from medical records. Second, the sample size was relatively small from a single medical center.

5 | CONCLUSIONS

Using ECMO in donations after DCD or DBD is an effective technique to increase organ pool. In the short term, the bilirubin levels poorly recovered when using ECMO preservation, but no patient experienced any ischemic-type biliary stricture complication after LT. Neither the DBD with ECMO group nor the DCD with ECMO group had significantly different short-term or long-term patient survival rates than the DBD group. This extracorporeal membrane oxygenation technique was utilized in our center, and expanded 35.6% ($n=32/90$) of the liver graft pool.

AUTHOR CONTRIBUTIONS

Concept and design: C.E.H., Y.L.H., Y.J.H., Y.L.C. Acquisition, analysis, or interpretation of data: C.E.H., H.R.L., K.H.L., W.Y.C., H.M.W., S.B.H. Drafting of the manuscript: Y.L.H., Y.J.H. Critical revision of the manuscript for important intellectual content: C.E.H., Y.L.H., Y.J.H., Y.L.C. Statistical analysis: C.E.H., Y.L.H. Supervision: Y.L.C.

ACKNOWLEDGMENTS

The authors would like to thank cardiovascular surgeon for assisting setting extracorporeal membrane oxygenation.

FUNDING INFORMATION

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest for this article.

ETHICS STATEMENT

The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution (Institutional Review Board of the Changhua Christian Hospital: No. CCH 191244), and it conforms to the provisions of the Declaration of Helsinki.

ORCID

Chia-En Hsieh https://orcid.org/0000-0002-8819-6989

REFERENCES

1. Steinbrook R. Organ donation after cardiac death. N Engl J Med. 2007;357:209–13.
2. Rao V, Dhanani S, MacLean J, Payne C, Paltser E, Humar A, et al. Effect of organ donation after circulatory determination of death on number of organ transplants from donors with neurologic determination of death. CMAJ. 2017;189:E1206–11.
3. Eren EA, Latchana N, Beal E, Hayes D Jr, Whitson B, Black SM. Donations after circulatory death in liver transplant. Exp Clin Transplant. 2016;14:463–70.
4. Meurisse N, Vanden Bussche S, Jochmans I, Francois J, Desschans B, Laleman W, et al. Outcomes of liver transplantations using donations after circulatory death: a single-center experience. Transplant Proc. 2012;44(9):2868–73.
5. Hsieh CE, Lin HC, Tsui YC, Lin PY, Lin KH, Chang YY, et al. Extracorporeal membrane oxygenation support in potential organ donors for brain death determination. Transplant Proc. 2011;43:2495–8.
6. Johnson LB, Plotkin JS, Howell CD, Njoku MJ, Kuo PC, Bartlett ST. Successful emergency transplantation of a liver allograft from a donor maintained on extracorporeal membrane oxygenation. Transplantation. 1997;63:910–1.
7. Lie SA, Hwang NC. Challenges of brain death and apnea testing in adult patients on extracorporeal membrane oxygenation-a review. J Cardiothorac Vasc Anesth. 2019;33:2266–72.
8. Shapiro BA. The apnea-$PaCO_2$ relationship: some clinical and medico-legal considerations. J Clin Anesth. 1989;1:323–7.
9. Bruce EN, Cherniack NS. Central chemoreceptors. J Appl Physiol (1985). 1987;62(2):389–402. https://doi.org/10.1152/jappl.1987.62.2.389
10. Maggi U, De Feo TM, Andorno E, Cillo U, De Carlis L, Colledan M, et al. Fifteen years and 382 extended right grafts from in situ split livers in a multicenter study: are these still extended criteria liver grafts? Liver Transpl. 2015;21(4):500–11.
11. Assalino M, Majno P, Toso C, Berney T, Giraud R, Dutkowski P, et al. In situ liver splitting under extracorporeal membrane oxygenation in brain-dead donor. Am J Transplant. 2018;18(1):258–61.
12. Dar WA, Sullivan E, Bynon JS, Eltzschig H, Ju C. Ischaemia reperfusion injury in liver transplantation: cellular and molecular mechanisms. Liver Int. 2019;39:788–801.
13. Cannistrà M, Ruggiero M, Zullo A, Gallelli G, Serafini S, Maria M, et al. Hepatic ischemia reperfusion injury: a systematic review of literature and the role of current drugs and biomarkers. Int J Surg. 2016;33:S57–70.
14. Guo Z, Zhao Q, Jia Z, Huang C, Wang D, Ju W, et al. A randomized-controlled trial of ischemia-free liver transplantation for end-stage liver disease. J Hepatol. 2023;23:1–9.
15. Bronchard R, Durand L, Legeai C, Cohen J, Guerrini P, Bastien O. Brain-dead donors on extracorporeal membrane oxygenation. Crit Care Med. 2017;45:1734–41.
16. Hackl C, Schmidt KM, Süsal C, Döhler B, Zidek M, Schlitt HJ. Split liver transplantation: current developments. World J Gastroenterol. 2018;24:5312–21.
17. Mihaylov P, Mangus R, Ekser B, Cabrales A, Timsina L, Fridell J, et al. Expanding the donor pool with the use of extended criteria donation after circulatory death livers. Liver Transpl. 2019;25:1198–208.
18. Fan X, Chen Z, Nasralla D, Zemg X, Yang J, Ye S, et al. The organ preservation and enhancement of donation success ratio effect of extracorporeal membrane oxygenation in circulatory unstable brain death donor. Clin Transplant. 2016;30:1306–13.

19. Cao Y, Shahrestani S, Chew HC, Crawford M, Macdonald PS, Laurence J, et al. Donation after circulatory death for liver transplantation: a meta-analysis on the location of life support withdrawal affecting outcomes. Transplantation. 2016;100:1513–24.
20. Lomero M, Gardiner D, Coll E, Haase-Kromwijk B, Procaccio F, Immer F, et al. Donation after circulatory death today: an updated overview of the European landscape. Transpl Int. 2020;33:76–88.
21. Schlegel A, Dutkowski P. Role of hypothermic machine perfusion in liver transplantation. Transpl Int. 2015;28:677–89.
22. Karangwa S, Panayotova G, Dutkowski P, Porte RJ, Guarrera JV, Schlegel A. Hypothermic machine perfusion in liver transplantation. Int J Surg. 2020;82S:44–51.
23. Martins PN, Buchwald JE, Mergental H, Vargas L, Quintini C. The role of normothermic machine perfusion in liver transplantation. Int J Surg. 2020;82S:52–60.
24. Lazzeri C, Bonizzoli M, Valente S, Cianchi G, Migliaccio ML, Gensini GF, et al. The role of extracorporeal membrane oxygenation in donation after circulatory death. Minerva Anestesiol. 2014;80:1217–27.

How to cite this article: Hsieh C-E, Hsu Y-L, Chen Y-L, Liang H-R, Lin K-H, Chen W-Y, et al. Using extracorporeal membrane oxygenation in donations after cardiac death or brain death: A single-center experience and long-term outcome. Ann Gastroenterol Surg. 2024;8:312–320. https://doi.org/10.1002/ags3.12749