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Organ Donation From Patients on Extracorporeal Membrane Oxygenation at the Time of Death

Nina A. Fainberg, MD[1]
Wynne E. Morrison, MD, MBE[1]
Sharon West, MS[2]
Richard Hasz, MFS[2]
Matthew P. Kirschen, MD, PhD[1]

OBJECTIVES: To describe the clinical characteristics and organ donation rate of patients supported by extracorporeal membrane oxygenation (ECMO) at the time of death.

DESIGN: Retrospective observational study. Pearson chi-square and Fisher exact tests were used in statistical analyses.

SETTING: One hundred twenty-seven acute care hospitals in New Jersey, Pennsylvania, and Delaware.

PATIENTS: Adult and pediatric patients who were on ECMO at the time of referral to a large organ procurement organization (OPO) between 2016 and 2020.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Nineteen thousand nine hundred thirty patients were referred to the OPO between November 2016 and September 2020, of which 5,034 were medically suitable potential donors. Of this cohort, 143 patients were supported on ECMO at the time of OPO referral and 141 were included in analyses (median age 47 yr, 60% male). Thirty-three percent (46/141, median age 48 yr, 52% male) donated organs, compared with 50% of non-ECMO patients ($p \leq 0.0005$). ECMO and non-ECMO patients had organs recovered but not transplanted at similar rates (11% vs 10%, $p = 0.8$). There were no significant differences in sex ($p = 0.16$) or ethnicity ($p = 0.50$) between organ donor and non-donor groups. Fifty-one percent (21/41) of organ donors donated after circulatory death and 49% (20/41) after brain death. Patients declared dead by neurologic criteria were more likely to donate (51%) than those declared dead by circulatory criteria (21%, $p < 0.001$). Frequency of cardiac arrest prior to ECMO was similar between donors and nondonors ($p = 0.68$). Thirty-nine percent (16/41) of donors had an out-of-hospital cardiac arrest (OHCA) and 51% (21/41) were cannulated via extracorporeal cardiopulmonary resuscitation (ECPR). The most common reason patients were not donors was that family declined (57%).

CONCLUSIONS: One-third of patients referred to the OPO on ECMO at the time of death donated organs. While donation occurred less frequently after ECMO, ECMO and non-ECMO patients had organs used rather than discarded at a similar rate. Patients successfully donated following OHCA and/or ECPR. Clinicians should not consider ECMO a barrier to organ donation.

KEY WORDS: brain death; end-of-life care; extracorporeal membrane oxygenation; organ donation; organ transplantation

The demand for organ transplantation outweighs the availability and has led to an international organ shortage crisis (1–4). In 2020, the waiting list for solid organs reached 178,077 in the United States, while only 39,913 organ transplantations were performed (3). Institutions have used several strategies to mitigate this problem, and elaborate organ recovery and

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KEY POINTS

Question: The goal of this study was to describe the clinical characteristics and organ donation rate of patients supported by extracorporeal membrane oxygenation (ECMO) at the time of death.

Findings: One-third of patients referred to a regional organ procurement organization who died on ECMO were organ donors. Although donation occurred less frequently after ECMO, ECMO and non-ECMO donors had organs transplanted rather than discarded at a similar rate. Events and procedures associated with high morbidity, including out-of-hospital cardiac arrest and extracorporeal cardiopulmonary resuscitation, did not preclude organ donation. Both donation after brain death and donation after cardiac death were suitable paths to donation.

Meaning: Clinicians should not consider ECMO a barrier to organ donation.

matching programs have been implemented worldwide to optimize organ availability, equity in organ distribution, and recipient survival.

Extracorporeal membrane oxygenation (ECMO) is a therapy for patients with cardiac and/or respiratory failure unable to be adequately supported by conventional means. Venovenous ECMO provides respiratory support, whereas venoarterial ECMO provides both respiratory and hemodynamic support (5). The past decade has seen exceptional growth in ECMO utilization, which more than quadrupled between 2010 and 2019 (6, 7). Rates of extracorporeal cardiopulmonary resuscitation (ECPR), in which venoarterial ECMO is deployed as a salvage procedure for patients in cardiac arrest, have risen in parallel (6). The use of ECMO as a rescue therapy has saved thousands of lives. At the same time, ECMO remains a highly invasive, resource-intensive procedure with a high mortality rate. Survival to decannulation varies widely based on indication for ECMO and type of cannulation but averages between 50% and 60% (6, 8–15).

Not all patients on ECMO have a positive outcome, but the opportunity to donate organs may offer a benefit to other patients and society even when the individual cannot survive. Donation can occur after a diagnosis of brain death (DBD) or after circulatory death (DCD) when ECMO support is terminated (16). There is a lack of standardization in determining death for patients on ECMO (16–20). Data on donation rates from patients supported by ECMO are limited to small single-center reports (2, 21, 22).

We aimed to describe the frequency of organ donation from patients supported by ECMO at the time of death using a large, regional organ procurement organization (OPO) database, and to compare patient characteristics between patients supported on ECMO who did and did not donate organs. Our intention was to bridge this knowledge gap by characterizing an underdescribed population of organ donors.

MATERIALS AND METHODS

This was a retrospective observational study of patients on ECMO at the time of referral to the Gift of Life Donor Program, a large regional OPO. The Gift of Life Donor Program database includes patients referred from 127 acute care hospitals in Pennsylvania, southern New Jersey, and Delaware. All data were abstracted from the Gift of Life Donor Program database. We selected patients who were on ECMO at the time of referral between November 2016 and September 2020 and were medically suitable for donation. We abstracted demographics including age, sex, race, premorbid conditions, primary diagnosis, ECMO characteristics, cause of death, and organ and tissue donation status. We also obtained information regarding number and types of organs transplanted and reasons donation did not occur. We excluded patients missing organ donation status and those who were not on ECMO at the time of death or withdrawal of technology. The Children's Hospital of Philadelphia Institutional Review Board (IRB) reviewed this study and waived the need for approval and informed consent due to use of decedents' personal health information only (IRB 20-017510, "Organ Donation Following ECMO," April 22, 2020). Procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975.

We categorized patients as organ donors and nondonors. We used the Organ Procurement and Transplantation Network (OPTN) definition of an organ donor as a patient who had at least one solid organ recovered for the purpose of transplantation (23). We treated donors who had organs recovered but not transplanted as nondonors in the analyses because successful transplantation was the outcome of interest.

We report descriptive statistics as percentages. Statistical comparisons were performed using the Pearson chi-square and Fisher exact tests. All statistical analyses were performed using Intercooled STATA software, Version 16.1 (College Station, TX).

RESULTS

We screened 19,930 patients referred for organ donation to the Gift of Life Donor Program between November 2016 and September 2020, of which 5,034 were medically suitable potential donors. In the cohort of medically suitable donors, 143 (3%) were supported on ECMO at the time of referral (median age 47 yr, 60% male). Two patients were excluded due to missing data and/or not being on ECMO at the time of death or withdrawal of technology. Of the remaining 141 patients on ECMO at the time of death, 46 (33%) donated organs. In comparison, 2,423 (50%) of 4,891 non-ECMO patients donated organs ($p \le 0.0005$). Five (11%) of the 46 intended donors on ECMO at the time of death had organs discarded prior to transplantation, compared with 250 (10%) of the 2,423 intended donors who were not on ECMO at the time of death ($p = 0.8$) These patients met criteria as organ donors based on the OPTN definition (23) but were treated as nondonors in the remainder of analyses as described above. Of the five patients on ECMO who had organs discarded, three died (60%) of brain death and two died (40%) by circulatory criteria. Organs were discarded based on assessment by the procuring surgeon or inability to find a suitable match. Of the remaining 41 patients who donated organs, 20 died (49%) of brain death and 21 died (51%) by circulatory criteria. Of the 100 patients who did not donate organs, 19 died (19%) of brain death and 81 (81%) by circulatory criteria (**Fig. 1**). Among all patients, those who were brain dead were more likely to donate than those who died by circulatory criteria (51% vs 21%; $p = 0.001$).

There were no significant differences between age ($p = 0.16$), sex ($p = 0.70$), or ethnicity ($p = 0.50$) between organ donors and nondonors (**Table 1**). Nondonors were more likely to have arterial hypertension as a premorbid condition ($p = 0.02$). There were no other significant differences between premorbid illnesses between donor and nondonor groups. Primary diagnoses did not differ between donor and nondonor groups (**Table 2**).

Eighty-seven organs were transplanted from the 41 organ donors. The most common were kidneys (n = 64, 74%) and livers (n = 11, 13%). Hearts were transplanted from two patients declared brain dead. No patients donated lungs, intestines, or pancreas. Tissue was procured from 16 (39%) donors, including 34 corneas, nine heart valves, and additional muscle, skin, and bone donations. The most common reason donation did not occur was that family declined (58, 58%). Twenty-nine patients (29%) who did not donate died before organ donation was discussed with the family. Five patients (5%) had organs procured but discarded, and one patient (1%) was declined by the medical examiner. Seven patients (7%) did not donate organs for reasons not documented.

Patients who donated organs experienced similar rates of pre-ECMO cardiac arrest compared with patients who did not donate organs ($p = 0.68$). Out-of-hospital cardiac arrests (OHCAs) occurred at a frequency similar to in-hospital cardiac arrests (IHCAs) among patients who donated organs ($p = 0.24$). The rates of OHCA and IHCA were similar between patients who did and did not donate organs ($p = 0.25$). Fifty-one percent of patients who donated organs were cannulated during cardiac arrest (i.e., ECPR). This rate of ECPR was similar to that of patients who were not organ donors (60%; $p = 0.35$). Type of ECMO cannulation (venovenous vs venoarterial) was similar between patients who did and did not donate organs ($p = 0.13$).

DISCUSSION

In this study using a large, regional OPO database, we found that one-third of referred potential donors on ECMO at the time of death donated organs. Patients with clinical characteristics typically associated with increased morbidity, such as those who had an OHCA, were on venoarterial ECMO, were cannulated via ECPR, and were able to donate organs. Only a small percentage (11%) of intended donors had organs discarded prior to transplantation. While donation was less common among patients on ECMO compared with those not on ECMO, organs between these groups were transplanted rather than discarded at a similar frequency. The most common reason donation did not occur was that families declined.

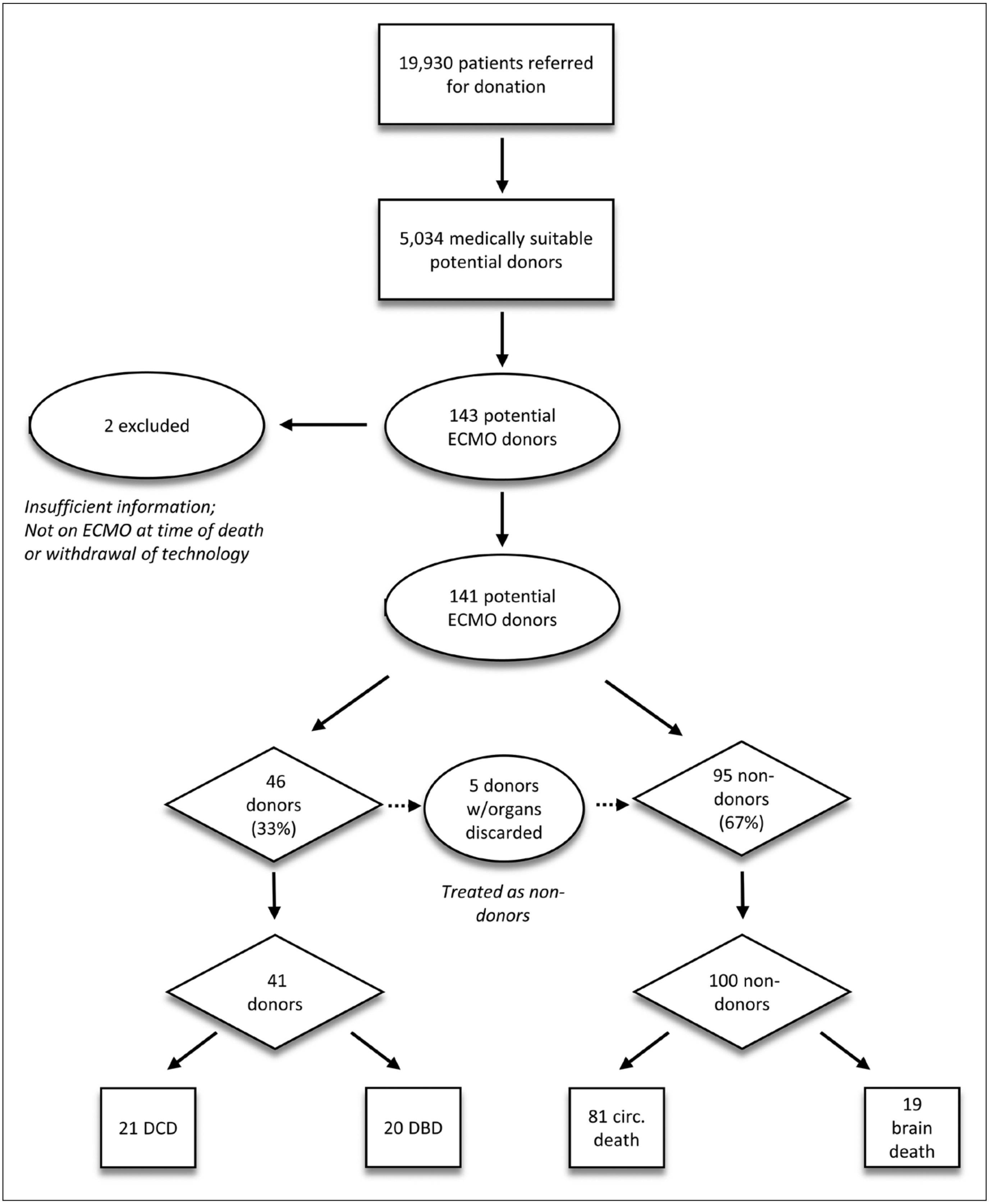

Figure 1. Flow diagram depicting the breakdown of patients on extracorporeal membrane oxygenation (ECMO) by donation status, cause of death, and mode of donation. circ. = circulatory, DBD = donation after brain death, DCD = donation after cardiac death.

TABLE 1.
Demographics of Patients on Extracorporeal Membrane Oxygenation at Time of Referral to Organ Procurement Organization

Characteristic	No. (%) Donor	Nondonor	p
Sex			
Male = yes	21 (52)	64 (64)	0.16
Age, yr			0.70
< 2	1 (2)	1 (1)	
2–17	3 (7)	7 (7)	
> 17	37 (91)	92 (92)	
Race/ethnicity			0.50
White	32 (78)	63 (63)	
Black/African American	5 (12)	21 (21)	
Hispanic/Latino	4 (10)	12 (12)	
Asian/Indian/ Pacific Islander	0 (0)	2 (2)	
American Indian/ Alaska Native	0 (0)	0 (0)	
Other/mixed/ unspecified	0 (0)	2 (2)	
Trauma = yes	1 (2)	4 (4)	1.00
Premorbid conditions			
Arterial hypertension	9 (22)	44 (44)	0.02
Diabetes mellitus	7 (17)	21 (21)	0.65
Obesity	19 (46)	37 (37)	0.35
Cancer	2 (4)	6 (6)	1.00
Respiratory disease	13 (32)	23 (23)	0.29
Acquired cardiovascular disease	9 (22)	39 (39)	0.08
Congenital cardiovascular disease	6 (15)	8 (8)	0.23
Renal insufficiency	1 (2)	6 (6)	0.67
Chronic neuro-logic disease	5 (12)	9 (9)	0.55

TABLE 2.
Primary Diagnoses of Patients on Extracorporeal Membrane Oxygenation at Time of Referral to Organ Procurement Organization

Primary Diagnosis	No. (%) Donor	Nondonor	p
Lung disease	13 (32)	20 (20)	0.19
Myocardial infarction	7 (17)	18 (18)	1.00
Cardiac arrest	7 (17)	20 (20)	0.82
Heart failure	3 (7)	16 (16)	0.28
Pulmonary embolism	3 (7)	8 (8)	1.00

Various strategies have emerged in recent decades to augment the donor pool. Expanded criteria for patients donating kidneys were developed to include those whose relative risk of graft failure is higher (24). DCD is now used more commonly as newer recovery and regional perfusion techniques minimize warm and cold ischemic times, including for transplanted hearts (1, 25–30). Additionally, organs are being considered when patients receive cardiopulmonary resuscitation (CPR) (i.e., uncontrolled donation after circulatory determination of death) or ECMO for the sole purpose of donation rather than as a life-saving intervention (2, 31, 32). Xenotransplantation, or cross-species transplantation, is being investigated in animal models (33, 34); in 2021, a kidney from a genetically modified pig was transplanted into a human recipient for the first time (35, 36).

Patients on ECMO may be ideal donor candidates as their organs are provided with physiologic support during their critical illness. Data regarding outcomes of organs transplanted from patients on ECMO are sparse. Bronchard et al (21) found similar graft function and recipient survival when organs were recovered from patients on ECMO compared with patients not on ECMO at the time of death. Similarly, Carter et al (22) found comparable graft survival of kidneys and livers. More information about organ donation practices and recipient outcomes from patients on ECMO could influence rates of referrals and acceptance of organs by transplant centers.

We found that conditions typically associated with high morbidity—including OHCA, ECPR, and veno-arterial ECMO—were equally prevalent in patients who did and did not donate organs. Patients who did and did not donate organs had similar demographics and clinical characteristics. The exception was arterial hypertension, which was more common in patients who were not organ donors. The association of hypertension with a higher rate of graft loss may impact acceptance of kidneys from hypertensive donors (37, 38). Fifteen percent of patients in our cohort had chronic neurologic disease, and 12 of these patients were able to donate organs. This is interesting because hospitals may consider a patient's preexisting neurologic disorder or baseline level of neurologic function when determining ECMO candidacy. Eight patients in our cohort had cancer as a preexisting condition, and two donated organs. The patients who donated had acute lymphoblastic leukemia and renal cell carcinoma, and donated a liver and kidney, respectively. They were considered in remission at the time of death. OPO referral by acute care hospitals is federally mandated for any patient whose death is expected to be imminent, but this practice is variable (3, 39). Research on perceptions of donation candidacy after ECMO is sparse and requires further investigation. Our data suggest that providers should not make assumptions about which patients on ECMO may or may not be acceptable donors.

Our donor cohort included patients donating after circulatory death and patients donating after brain death, demonstrating that both paths to donation are feasible for ECMO patients. Interestingly, patients declared brain dead while on ECMO were more likely to be donors than those not declared dead before removal of technology. There are several reasons why this may have occurred. First, the Gift of Life Donor Program sees a lower authorization rate for DCD potential donors compared with DBD potential donors due to families declining. This could contribute to a higher proportion of patients who died by circulatory criteria in the nondonor group. Second, since a DCD process requires withdrawing technology prior to donation, these patients may have been seen as more complicated logistically. Determining brain death in patients on ECMO also presents unique challenges, including unpredictable pharmacokinetics of drugs that may confound the brain death examination, and technical challenges in completing the apnea test (16). In light of these difficulties, there have been initiatives to standardize determination of death by neurologic criteria for ECMO patients (20, 40). Implementation of protocols for brain death determination on ECMO may increase the number of patients on ECMO assessed for organ donor candidacy.

The most common reason patients on ECMO did not donate was that their families declined. The reason warrants further investigation but may be partly explained by the higher proportion of DCD potential donors in the nondonor group. Discussing organ donation with families can be challenging for healthcare professionals, and the skill with which providers approach families has been identified as a key influence on the decisions to donate (41, 42). Other factors found to affect the decision to donate include timing of the approach, perceived quality of care of the patient, and the setting in which the request is made, with evidence that a private location increases consent rates (42). The past decade has seen numerous interventions aimed at healthcare professionals to increase the number of organ donors. Successful programs have focused on specialized communication training for providers, designating trained personnel to lead donation conversations, and improving collaboration between providers and OPOs (41–43). The second most common reason that donation did not occur was that withdrawal of life-sustaining therapies or death despite maximal interventions preceded the opportunity to discuss donation with the family. Interventions could be considered to improve identification of patients on ECMO as potential donors and expedite OPO referral.

Transplant centers have flexibility to accept or deny organs on a case-by-case basis based on evaluations of organ suitability. While ECMO is associated with substantial morbidity, only 11% (5/46) of intended donors had organs discarded rather than transplanted based on procuring surgeons' assessments and/or ability to find a suitable match. This rate did not differ significantly from patients not on ECMO at the time of death. Although patients on ECMO are some of the most critically ill in the hospital, our findings suggest that their organs are often acceptable for donation. These data align with existing studies that have examined organ function following transplant from patients on ECMO at the time of death (21, 22). Emerging organ preservation technologies, such as ex situ organ perfusion, have shown promise in optimizing organ viability and graft function (44). These techniques may further enhance availability of organs from donors on ECMO at the time of death.

ECMO is a highly invasive and resource-intensive procedure aimed at bridging patients to recovery and a meaningful quality of life (45). Determining ECMO candidacy is provider- and institution-dependent. Different guidelines exist for distinct patient populations, but there are no universal recommendations (45–47). The decision to cannulate ECMO often occurs emergently, where the calculated risk-benefit ratio may be influenced by stress and other psychoemotional factors (48). Uncontrolled donation and regional perfusion protocols have used CPR and extracorporeal support for a different purpose: as a bridge to donation rather than as a life-saving therapy. This has been ethically criticized because of the sometimes rapid shift from a focus on saving the patient to a focus on donation (49–51). At the same time, when life-sustaining measures are deemed futile, the opportunity to donate organs can present families with something meaningful to come out of their loss. Organ donation may be an under-recognized benefit of ECMO and ECPR, although it is not a traditional measure of a positive outcome. The question of whether the potential to donate should impact ECMO candidacy warrants further ethical consideration.

Our study had limitations. This was a retrospective review of a regional OPO database and results may not be generalizable to a larger population or a different region. Our OPO database is reliant on provider referrals, and thus we may miss patients on ECMO who were not referred. It is possible that we overestimated the rate at which patients on ECMO donate organs, although this is less likely because referral is mandated. The database is populated via manual entry by OPO coordinators, which may impact its accuracy and completeness. For the patients who had organs procured and deemed unacceptable for transplant, the reasons are unknown. Organ suitability could have been affected by the patient's primary pathophysiology, from the ECMO procedure (e.g., due to clot formation and embolization), or a combination. Further research is needed to delineate the risks of ECMO itself on suitability of organs for transplantation. Finally, we did not examine the outcome of organ recipients who received organs from donors on ECMO at the time of death and cannot comment on graft function or survival in recipients. Information about outcomes could better inform those considering patients on ECMO as organ donors and would be a topic for future research.

CONCLUSIONS

One-third of patients supported on ECMO at the time of their death donated organs. Although patients on ECMO donated less frequently than patients not on ECMO, rate of organ utilization after procurement did not differ between these groups. Patients who sustained OHCA and were cannulated via ECPR were suitable organ donors. Those declared brain dead were more likely to donate organs than those who were not. Consideration of patients on ECMO for organ donation can provide a benefit to families of these patients, as well as to potential organ recipients who may otherwise die awaiting transplant. Providers should not consider ECMO a barrier to organ donation.

1 Department of Anesthesiology and Critical Care Medicine, Children's Hospital of Philadelphia, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA.

2 Gift of Life Donor Program, Philadelphia, PA.

Ms. West and Mr. Hasz are employed by the local organ procurement organization whose database was used for this study (Gift of Life Donor Program, Philadelphia, PA). The remaining authors have disclosed that they do not have any potential conflicts of interest.

For information regarding this article, E-mail: fainbergn@chop.edu

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