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Review

Organ Donation after Extracorporeal Cardiopulmonary Resuscitation: Clinical and Ethical Perspectives

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Extracorporeal cardiopulmonary resuscitation (ECPR) has evolved into a life-saving therapy for select cardiac arrest patients, yet a growing body of evidence suggests it also holds promise as a bridge to organ donation in non-survivors. This review explores the clinical outcomes, ethical complexities, and evolving policies surrounding organ donation after ECPR. We summarize recent international and Japanese data demonstrating favorable graft function from ECPR donors, with the exception of lung transplantation. The ethical challenges — particularly those involving brain death determination on extracorporeal membrane oxygenation and adherence to the dead donor rule — are discussed in the context of Japan's recent regulatory reforms. Additionally, we highlight the importance of structured end-of-life communication through multidisciplinary team meetings in facilitating ethically sound transitions from rescue efforts to donation pathways. Moving forward, improvements in donor management, standardized legal frameworks, and public and professional education are essential to optimizing the life-saving and life-giving potential of ECPR.

Key words: brain death, end-of-life care, ethical dilemmas, extracorporeal cardiopulmonary resuscitation

Organ transplantation is a life-saving intervention for patients with end-stage organ failure. However, the global demand for donor organs far exceeds the available supply, due in part to improvements in the management of chronic organ failure, advances in transplantation techniques, and extended post-transplant survival [1]. In response to this growing shortage, various strategies have been implemented worldwide to increase organ donation, including the early identification of potential donors, enhancement of public awareness, and the development of national organ procurement systems [2, 3].

Cardiac arrest is one of the most common causes of devastating brain injury and may lead to brain death, thereby creating the potential for deceased organ donation [4]. Extracorporeal cardiopulmonary resuscitation (ECPR) — the application of extracorporeal membrane oxygenation (ECMO) during cardiopulmonary resuscitation — has emerged over the past two decades as an advanced resuscitative technique for selected patients with cardiac arrest due to potentially reversible causes [5]. While ECPR may improve survival in carefully selected patients, it also introduces complex ethical considerations, particularly when patients fail to recover neurologically and subsequently become candidates for organ donation [6, 7]. Japan has one of the lowest deceased organ donation rates among developed countries [8]. Paradoxically, Japan is also a global

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leader in the implementation of ECPR [5], raising unique ethical and societal challenges related to the potential overlap between resuscitative efforts and organ donation pathways.

In this review, we explore the intersection of ECPR and organ donation, highlighting current challenges and future directions. We also examine the ethical implications, with particular emphasis on respecting patient autonomy and family preferences in end-of-life decision-making.

Deceased Organ Donation Worldwide

Deceased organ donation — the recovery of organs from individuals declared dead based on neurological or circulatory criteria — is a major source of transplantable organs [9]. This includes donation after brain death (DBD), based on irreversible loss of all brain function, and donation after circulatory death (DCD), following irreversible cessation of cardiac and respiratory activity. DBD donors are particularly important for heart, lung, liver, and kidney transplants, while DCD donors increasingly contribute kidneys and select other organs.

Globally, the rate of deceased organ donation — comprising both DBD and DCD — varies substantially between countries. According to the most recent data from 2022, Spain remains the global leader in deceased organ donation, reporting 47.0 deceased donors per million population (pmp), followed closely by the U.S. at 44.5 pmp <http:www.transplant-observatory.org (accessed April 29, 2025)>. These rates are considerably higher than those observed in most other countries. For example, France reported 25.8 deceased donors pmp, and the UK 21.1 pmp in the same year. In contrast, Japan recorded only 0.9 deceased donors pmp, placing it among the lowest rates within developed nations — nearly nine times lower than South Korea's rate of 7.9 pmp.

Prevalence of Living Organ Donors

Living organ donation plays a vital role in addressing organ shortages, though its use varies widely across countries. Japan is among the most reliant, with 14.5 living donors pmp in 2022, and over 80% of all transplants derived from living donors [10] <https://worldpopulationreview.com/country-rankings/organ-donation-rates-by-country. (accessed April 29, 2025)> — a reflection of its persistently low deceased donor rate. In contrast, the U.S. reported 19.3 living donors pmp, comprising about 30% of all donors, with living donation contributing substantially to kidney and liver transplantation. Most European countries prioritize deceased donation. France recorded 8.2 living donors pmp, the UK 12.9 pmp, and Spain — despite leading in deceased donation — reported only 7.4 pmp, with living donors accounting for just 13% of the total <https://worldpopulationreview.com/country-rankings/organ-donation-rates-by-country. (accessed April 29, 2025)>.

Common Causes of Brain Death Leading to Organ Donation

Brain death leading to organ donation typically results from catastrophic neurological events that cause irreversible cessation of all brain function. The most common causes include severe traumatic brain injury, hemorrhagic stroke (such as intracerebral or subarachnoid hemorrhage), and prolonged global ischemia or anoxia, often due to cardiac arrest or drug overdose [11]. These conditions lead to diffuse cerebral edema, elevated intracranial pressure, brainstem herniation, and ultimately cessation of cerebral perfusion. While massive ischemic strokes (*e.g.*, large middle cerebral artery infarctions) may also result in brain death, they occur less frequently than hemorrhagic events. The distribution of these causes varies by country, reflecting differences in population demographics, healthcare systems, and public health challenges, including stroke prevalence, trauma incidence, and substance use patterns.

In the U.S., data from 2019 showed that anoxic brain injury was the leading cause of brain death among organ donors, accounting for 45.0% of cases, followed by stroke at 26.3% and head trauma at 25.4%. Other causes, such as central nervous system tumors and unknown etiologies, represented less than 3.2% combined [12]. In Spain, data collected between January 1, 2010 and June 30, 2012 revealed that intracerebral hemorrhage accounted for 42% of brain death cases among organ donors. This was followed by traumatic brain injury (19%), subarachnoid hemorrhage (14%), anoxic encephalopathy (9%), and ischemic stroke (9%). Additional causes included road traffic collision-related trauma (7%), other trauma (12%), brain tumors (2%), and other causes (5%). These figures emphasize the predominance of cerebrovascular events in Spain's donor population [13]. In Japan, among 1, 150 brain-dead donors from October 16, 1997 to December 31, 2024, stroke was the most frequent cause in 502 (44%), followed by anoxic encephalopathy in 358 (31%) and traumatic brain injury in 172 (15%) <https://www.jotnw.or.jp/data/brain-death-data.php. (access April 29, 2025)>.

Anoxic encephalopathy, typically resulting from cardiac arrest, can lead to brain death. Japanese data showed that among 370 brain-dead donors who experienced cardiac arrest, the most common precipitating cause was hanging in105 cases (28%), followed by subarachnoid hemorrhage in 90 (24%), asphyxia due to foreign body in 32 (9%), cardiogenic causes such as acute myocardial infarction or fatal arrhythmia in 31 (8%), and traumatic brain injury in 21 (6%) [14].

Extracorporeal Cardiopulmonary Resuscitation

ECPR refers to the initiation of veno-arterial ECMO (VA-ECMO) during ongoing CPR in patients with cardiac arrest refractory to conventional measures. Over the past two decades, ECPR has evolved from an experimental rescue technique into a sophisticated resuscitative modality, largely due to technological advancements in portable ECMO systems and perfusion management [5, 15, 16]. ECPR is generally indicated for patients with cardiac arrest due to a potentially reversible cause, particularly when traditional CPR fails to restore spontaneous circulation. Ideal candidates include individuals with witnessed arrests, brief low-flow times (typically under 60 min), and reversible etiologies such as acute coronary syndrome, pulmonary embolism, malignant arrhythmias, severe hypothermia, or toxin-induced cardiac arrest [17, 18].

Japan has played a pivotal role in advancing the clinical implementation of ECPR. A landmark prospective study in 2014 demonstrated significantly improved survival among out-of-hospital cardiac arrest (OHCA) patients treated with ECPR compared to conventional CPR [19]. A subsequent large-scale cohort study from Japan reported survival to hospital discharge in 27.2% and favorable neurological outcomes in 14.1% of ECPR-treated OHCA patients [20]. These outcomes are substantially higher than those observed in the general OHCA population, for whom recent national data show 1-month survival and neurologically favorable outcomes of approximately 2.5% and 5.4%, respectively [21]. Furthermore, nationwide trends suggest increasing utilization of ECPR in Japan and a gradual improvement in outcomes over time, reflecting advances in patient selection and post-resuscitation care [22].

Organ Donation after ECPR

Importantly, ECPR may also enhance the potential for organ donation in patients who do not recover neurologically [23]. A meta-analysis found that the incidence of brain death among non-survivors was significantly higher in ECPR patients compared to conventional CPR (27.9% vs. 8.3%; $p < 0.0001$), and the overall rate of organ donation among brain-dead patients was approximately 42% [4].

Real-world data from European trials support these findings. In the Prague OHCA trial, 21 of 24 organ donors originated from the ECPR group, compared to only 3 from the non-ECPR group. Thirteen brain-dead donors in the ECPR arm contributed to the successful transplantation of 36 solid organs into 34 recipients, all of whom experienced excellent graft function at one year [24]. Similarly, in a large Italian cohort of 307 refractory OHCA patients treated with ECPR, 83% died during hospitalization, and 33% were diagnosed with brain death. At least one solid organ was donated by 58 patients (19%), predominantly after the determination of brain death. This contributed 167 transplantable organs — averaging 3 organs per donor — and resulted in benefit for nearly 200 individuals, including both transplant recipients and neurologically intact survivors [25]. Based on nationwide data from Japan, of 370 brain-dead donors following cardiac arrest, 26 (7.0%) received ECPR while 344 (93.0%) did not. The median number of organs donated was 5 in both groups [14].

Recent data suggest that ECPR non-survivors may serve as a meaningful donor source. In a single-center study from the U.S., 38 out of 303 non-survivors (13%) became organ donors, resulting in 74 transplants, an increase that paralleled the program's growing maturity [26]. While such data are limited in Japan [27], the recent approval of brain death determination under ECMO (discussed below) may help realize similar potential.

Recipient Outcomes from Donors after ECPR

Several registry studies have shown that ECPR patients who progress to brain death can be viable organ donors. A nationwide Japanese cohort reported no significant differences in long-term outcomes for recipients of kidney, liver, pancreas, or heart from ECPR donors compared to non-ECPR donors, though lung graft survival was lower—likely due to injury from cardiac arrest or prolonged ECMO [14]. This underscores the importance of careful pulmonary graft evaluation. European data similarly support the use of ECPR donors. One registry study noted that many non-surviving ECPR patients were successfully converted into organ donors, with follow-up confirming excellent graft function when preservation protocols were rigorously applied [28,29]. An additional consideration is the extended ICU stay seen among ECPR donors, especially in Japan. A recent national study found that the time from admission to procurement was significantly longer in ECPR cases [14] (Fig. 1). While this places greater demands on ICU resources, it also allows for thorough donor management and organ optimization [30].

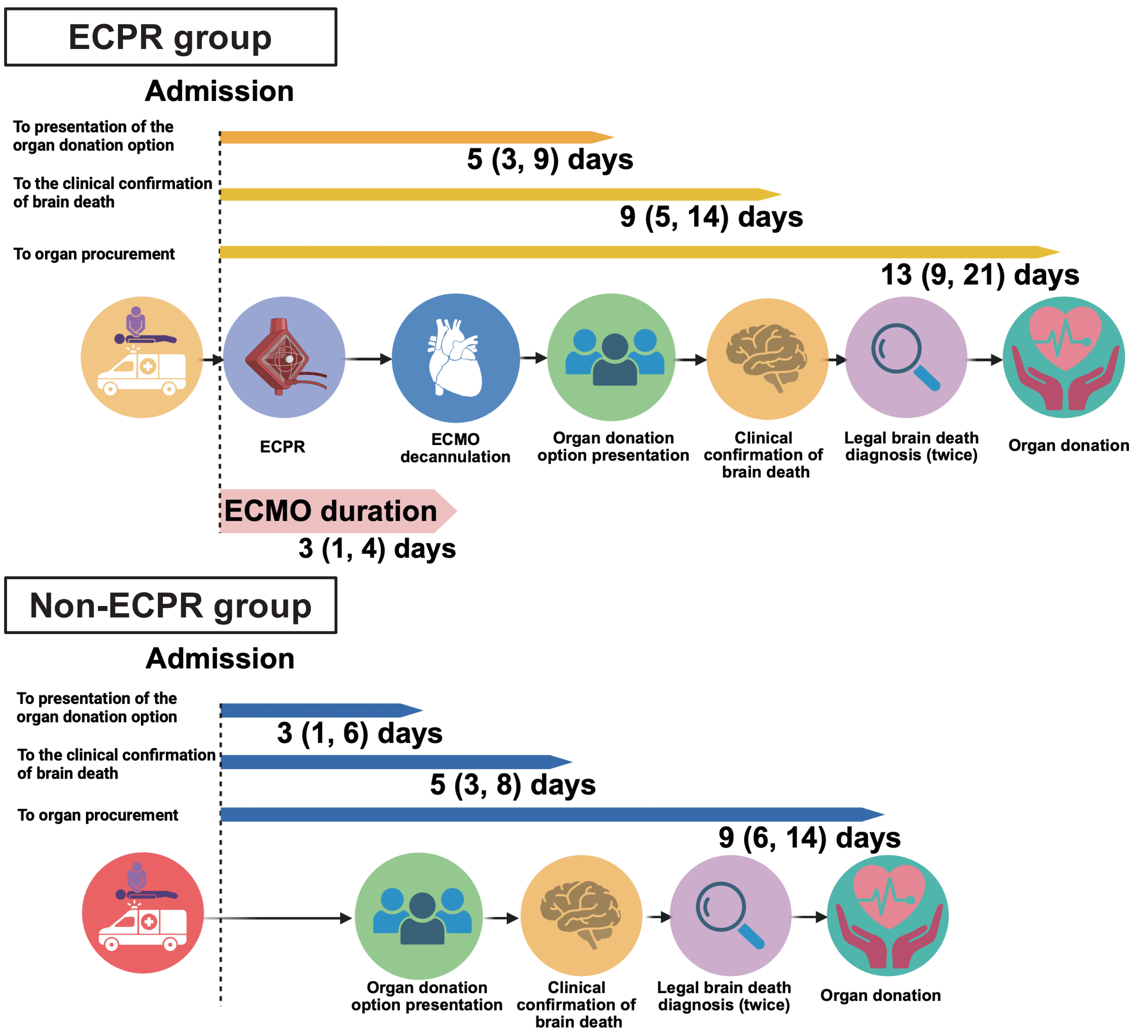

Fig. 1 Timeframe from admission to organ procurement between the ECPR group and non-ECPR group. Compared to non-ECPR patients, those who underwent ECPR had significantly longer intervals from admission to the presentation of the organ donation option to their families, to the clinical confirmation of brain death, and ultimately to organ procurement. Data are presented as medians with interquartile ranges. Figure revised from *Okayama Igakkai Zasshi*. 2025; 137(3).
ECPR, extracorporeal cardiopulmonary resuscitation.

It should also be noted that prolonged ECMO support complicates the assessment of transplantability for certain organs, particularly the heart and lungs. Functional evaluations — such as echocardiography or pulmonary compliance tests — may be limited by the physiological effects of extracorporeal circulation, potentially leading to lower utilization rates despite technically retrievable organs.

Ethical Issues on Organ Donation after ECPR

Using ECPR as a bridge to organ donation raises multifaceted ethical and legal questions [31,32]. Central to these is the dead donor rule, which mandates that organ procurement must not cause the donor's death and can only occur after death is declared by accepted criteria. In ECPR cases, patients may have restored circulation via ECMO despite a non-functioning brain, complicating the determination of death. Brain death (irreversible cessation of all brain function) is the usual pathway to declare death in such scenarios, but this requires a legal framework that permits brain-death testing even with circulatory support. Notably, until recently, Japan did not explicitly permit brain death determination while a patient was on ECMO, as there were no regulatory provisions addressing this situation. As a result, brain death diagnosis was not conducted under ECMO support in practice. Consequently, ECPR patients in Japan were generally eligible for organ donation only after ECMO withdrawal and subsequent circulatory arrest (*i.e.*, donation after circulatory death). However, recent amendments to the relevant guidelines in January 2024 have addressed this gap, and now allow for brain death determination under ECMO support in Japan [14]. This change brings Japan in line with international practice and upholds the dead donor rule by ensuring that death can be properly pronounced (via neurologic criteria) even if circulation is artificially maintained. In all jurisdictions, it remains imperative that death is unequivocally established by either neurologic or circulatory criteria before organ retrieval begins. Adhering to these principles is critical to maintain public trust in transplantation and to ensure that no violation of ethical norms occurs in the pursuit of organs.

One technical challenge in ECPR cases is differential hypoxemia under peripheral VA ECMO, where upper-body — including cerebral — perfusion may be insufficient. This phenomenon can theoretically hinder accurate brain death determination, as cerebral hypoxia could either mimic or mask irreversible injury [33]. In recent years, switching from VA ECMO to V-VA ECMO has been explored as a method to address this issue, but its implications for brain death diagnostics under ECMO raise nuanced ethical and clinical questions [34].

Determining futility and timing of withdrawal. A key ethical challenge in ECPR is determining when continued support is futile [6]. Since ECPR is initiated with the goal of saving a life, transitioning to end-of-life care can be emotionally and ethically sensitive. Clinicians must rely on prognostic indicators — such as absent brainstem reflexes, catastrophic brain injury, and prolonged no-flow time — to assess the likelihood of neurological recovery. A recent Japanese study reported that decisions to withdraw life-sustaining therapy often occur within 1 to 3 days after ECPR initiation when prognosis is poor [7]. Once it is concluded that ongoing treatment offers no benefit, the focus should shift to ensuring a dignified death and, if desired, discussing the option of organ donation. Crucially, the decision to withdraw ECPR must be made independently of organ donation considerations, to avoid any conflict of interest. Treating physicians should base this decision solely on medical futility, without influence from transplant teams. Only after withdrawal is clearly decided and documented should discussions about donation be initiated. This two-step process — first declaring futility, then exploring donation — preserves ethical integrity and the primary focus on the patient's best interests. Proper declaration of death is also essential. For brain death, a complete examination (including apnea testing) must be performed, even if the patient is on ECMO. For DCD, protocols require a mandatory waiting period after ECMO withdrawal to confirm irreversible asystole before restarting organ perfusion. These steps are vital to uphold the dead donor rule and ensure legal and ethical compliance [18,35].

While raising the topic of organ donation soon after a failed resuscitation attempt is delicate, studies suggest that many families are receptive to the discussion when approached properly [36]. Surveys of public opinion indicate that a majority of people would consider donation even in the emergency setting, and actual consent rates in sudden death scenarios can be equal to or higher than in anticipated end-of-life situations. The key is a sensitive, patient-centered approach—acknowledging the family's grief, respecting their wishes (including the right to decline), and framing organ donation as a voluntary opportunity to create something positive from tragedy.

Balancing patient best interests and organ preservation. A central ethical question in ECPR-to-donation cases is whether it is justifiable to continue life-sustaining or organ-preserving interventions when they no longer serve the patient's best interest [37-40]. Critics argue that once neurological devastation is confirmed, further invasive treatments—such as ECMO or medications—may violate the patient's dignity if not previously consented to, reducing the individual to an organ source. However, many ethicists support a more nuanced view: if the patient is legally dead or imminently dying, and if donation aligns with their values or prior wishes, continuing support briefly to facilitate donation can be consistent with honoring the patient's best interest. In such cases, structured interdisciplinary dialogue becomes essential [41,42]. Multidisciplinary team meetings, particularly ad hoc sessions involving physicians, nurses, social workers, and other specialists, offer a vital platform for collaborative end-of-life decision-making. These discussions enable the team to assess prognosis, clarify goals of care, and ensure that ongoing interventions remain consistent with the patient's values. Within the time-sensitive and ethically charged ICU setting, such dialogue fosters transparency, alleviates moral distress among clinicians, and helps build consensus with families. In patients who are brain-dead, maintaining organ function causes no harm and may be seen as a way of honoring their legacy. In DCD scenarios, brief circulatory support is ethically acceptable once death has been confirmed and appropriate consent obtained—so long as established protocols are followed, and the patient's best interest remains the guiding principle.

Differentiating DCD use of ECMO in organ preservation. While ECMO is used during ECPR to restore circulation, its application in controlled DCD (cDCD) differs significantly in intent and ethical implications. In cDCD, ECMO may be reinitiated postmortem for organ preservation—most notably in normothermic regional perfusion (NRP)—to reperfuse abdominal or thoracic organs while excluding cerebral circulation [32]. However, ethical concerns have been raised about inadvertent brain reperfusion through collateral vessels, which could undermine the validity of circulatory death determination. This is particularly debated in countries where legal definitions of death are based on irreversible cessation of brain function [43]. Globally, DCD with ECMO has gained traction, especially in heart transplantation, using either NRP or direct procurement and perfusion. As Japan explores DCD heart transplantation, it will be essential to distinguish this approach from ECPR-initiated support and ensure that any use of ECMO in DCD complies with clearly defined ethical and legal standards.

Future Directions

In the coming years, integrating ECPR with organ donation will require concerted efforts across the domains of clinical research, policy development, and education. First, targeted clinical studies are needed to optimize donor management and improve graft outcomes, especially for organs like the lungs that show reduced survival after ECPR. Ongoing research should focus on refining perfusion techniques, mitigating injury from prolonged ECMO, and monitoring long-term recipient outcomes. Second, legal and ethical frameworks must continue to evolve. Clear policies—such as Japan's recent approval of brain death determination on ECMO—provide a model for other regions to clarify the dead donor rule under advanced life support. Further consensus on DCD under ECMO is needed so that uncontrolled donation after circulatory death can be ethically and logistically feasible. Third, hospitals and transplant networks should establish robust institutional protocols for ECPR-linked donation, including standardized brain-death testing on ECMO and guidelines for timely withdrawal of support when appropriate. Finally, public and professional education is crucial. Training healthcare teams to approach families with sensitivity and transparency can improve consent rates, and broader community outreach can build trust in the dual purpose of ECPR as a life-saving and life-giving intervention.

There is also a lack of comprehensive data on hospital-level donation practices, management strategies, and procedural workflows in Japan. To address this, we established the Japan Comprehensive Process for End-of-Life Care and Organ Donation after Brain Death (J-RESPECT) study group, which aims to provide insights into procedural, institutional, and resource-

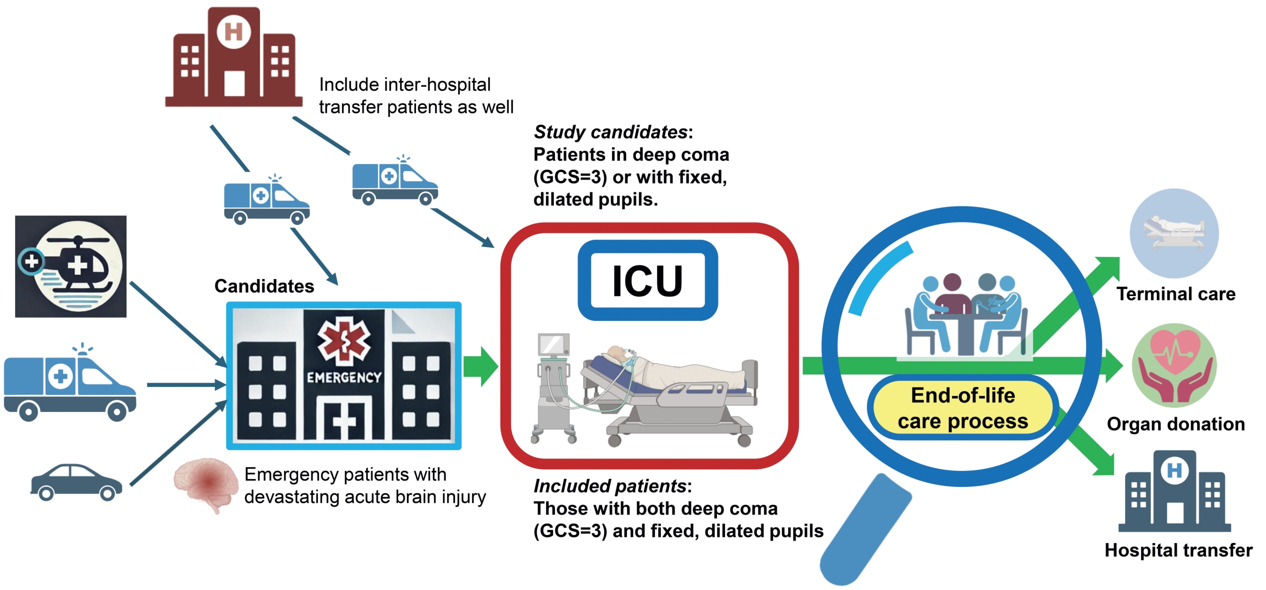

Fig. 2 Overview of the J-RESPECT 2 study. This prospective observational study is designed to examine the end-of-life care process, including organ donation, in patients with devastating acute brain injuries—specifically those presenting with both deep coma and fixed, dilated pupils.
ICU, intensive care unit; GCS, Glasgow Coma Scale.

related factors. A multicenter retrospective study is currently underway (UMIN000054415). Additionally, a prospective study is planned to examine the trajectory of end-of-life care, including the organ donation process, in patients with devastating brain injuries who are considered potential donors. This research will help identify institutional, individual, and clinical management factors contributing to variability in care, potentially informing improvements both within Japan and in other countries facing similar challenges (Fig. 2).

Conclusions

ECPR sits at a unique intersection of resuscitation and organ donation, offering a dual opportunity to save lives—first the patient's, then potentially others through transplantation. This review highlights that, with careful application, ECPR can support organ donation without compromising ethical standards or patient dignity. Integrating ECPR into donation pathways presents challenges: clinicians must navigate complex end-of-life decisions, uphold the dead donor rule, and coordinate within legal constraints. Yet recent progress, especially in Japan's alignment of brain death criteria with ECMO support, demonstrates positive momentum. With evolving protocols, ethical clarity, and collaborative education, ECPR's full potential can be realized—strengthening both advanced life support outcomes and the organ donation system.

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