CHEST Medical Ethics

Ethical Dilemmas Encountered With the Use of Extracorporeal Membrane Oxygenation in Adults

Darryl C. Abrams, MD; Kenneth Prager, MD; Craig D. Blinderman, MD; Kristin M. Burkart, MD; and Daniel Brodie, MD

Extracorporeal membrane oxygenation (ECMO) can serve as a bridge to recovery in cases of acute reversible illness, a bridge to transplantation in circumstances of irreversible cardiac or respiratory failure, a bridge to ventricular assist device therapy in select cases of cardiac failure, or a bridge to decision when the prognosis remains uncertain. Recent advances in ECMO technology that allow for prolonged support with decreased complications, the development of mobile ECMO teams, the rapidity of initiation, and the growing body of evidence, much of which remains controversial, have led to a significant increase in the use of ECMO worldwide. This increasing use of a technology that is not a destination device in itself introduces many ethical dilemmas specific to this technology. In this article, we explore some of the ethical issues inherent in the decisions surrounding the initiation and withdrawal of ECMO by raising key questions and providing a framework for clinicians. We will address extracorporeal cardiopulmonary resuscitation, the inability to bridge a patient to transplant or recovery—the so-called "bridge to nowhere"—and the significance of resuscitation preferences in the setting of continual extracorporeal circulatory support. ***CHEST 2014; 145(4):876–882***

Abbreviations: DNR = do not resuscitate; ECMO = extracorporeal membrane oxygenation; ECPR = extracorporeal CPR; VAD = ventricular assist device

Extracorporeal membrane oxygenation (ECMO) refers to an extracorporeal circuit through which blood is oxygenated and CO_2 is removed. With current technology, severe respiratory or cardiac failure may be either partially or completely supported with ECMO. Advances in extracorporeal technology and techniques as well as the creation of mobile ECMO teams that can retrieve and transport patients on the mechanical device have contributed to the expansion of its use worldwide.[1,2] The ability of ECMO to replace the function of the heart or lungs, and to do so rapidly and for prolonged periods of time, allows ECMO to be used as a bridge to recovery in cases of potentially reversible organ failure, a bridge to transplant in cases of end-stage cardiac or respiratory failure, a bridge to device therapy in select cases of cardiac failure, or a bridge to decision when the prognosis remains uncertain, for instance, when used in cardiac arrest, referred to as extracorporeal CPR (ECPR) (Fig 1).[3-7] Given the numerous potential applications for ECMO in critically ill patients, ethical issues will inevitably emerge regarding its appropriate initiation and management.

The concept of extracorporeal device-based therapy for providing organ support is not new. The ventricular assist device (VAD), used to support refractory heart failure, is comparable to ECMO in that it can provide significant circulatory support, and ECMO may serve as a bridge to VAD therapy. However, in

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Affiliations: From the Division of Pulmonary, Allergy, and Critical Care (Drs Abrams, Prager, Burkart, and Brodie) and the Center for Supportive Care and Clinical Ethics (Drs Prager and Blinderman), Department of Medicine, Columbia University College of Physicians and Surgeons, New York, NY.
Correspondence to: Daniel Brodie, MD, Columbia University College of Physicians and Surgeons, Division of Pulmonary, Allergy, and Critical Care, Department of Medicine, 622 W 168th St, PH 8E 101, New York, NY 10032; e-mail: hdb5@columbia.edu

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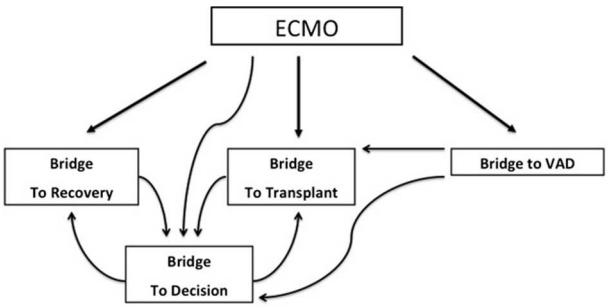

FIGURE 1. Decision tree for ECMO in cardiac or respiratory failure. ECMO = extracorporeal membrane oxygenation; VAD = ventricular assist device.

patients with refractory respiratory failure, no destination device option currently exists, meaning that patients receiving ECMO support are necessarily confined to the ICU. Circumstances may arise when a patient receiving ECMO is unable to be bridged to recovery, transplant, or destination device therapy, yet the patient is capable of surviving with ongoing ECMO support. Such an ethically challenging and emotionally charged situation is sometimes referred to as a "bridge to nowhere," with obvious implications for the patient, his or her family, the caregivers, the hospital, and the health-care system. Addressing the ethical issues that accompany ECMO becomes even more essential as the medical community has seen a significant expansion in case volume, due in part to the ease with which it can be initiated.[1] Despite its increased use, data regarding its efficacy are limited. The strongest evidence supporting ECMO for respiratory failure comes from the randomized controlled trial Efficacy and Economic Assessment of Conventional Ventilatory Support Versus Extracorporeal Membrane Oxygenation for Severe Adult Respiratory Failure (CESAR), which evaluated the use of venovenous ECMO for severe hypoxemic respiratory failure.[8] Although one may conclude that referral to an ECMO-capable center improves survival over conventional management at non-ECMO centers, methodological flaws limit the interpretation of this trial. Other evidence supporting the use of venovenous ECMO is limited to randomized trials with outdated technology or observational studies,[9-14] with propensity analyses demonstrating mixed results.[3,15,16] The data for venoarterial ECMO for ECPR, cardiac failure, and bridge to transplantation are even more limited.[4,5,7,17-20] The use of resource-intensive technology in the absence of data that establish a clear benefit raises ethical issues and, to some degree, requires a societal judgment on the acceptable use of expensive, unproven interventions. This issue is mitigated to some degree by the context in which ECMO is applied. For hypoxemic respiratory failure, it remains a salvage therapy for those unable to be managed with conventional support, with a multicenter randomized controlled trial currently underway to better define its role (ECMO to Rescue Lung Injury in Severe ARDS [EOLIA]).[21] In cases where ECMO serves as a bridge to lung transplantation, randomized trials of ECMO vs invasive mechanical ventilation are difficult to design because of the inevitability of death in those patients in whom ECMO is believed to be the only salvage option.[22] We are, therefore, left with observational studies that have inherent limitations in determining efficacy, although such studies have recently demonstrated improved posttransplant outcomes with ECMO as bridging therapy.[23,24] Ultimately, more data, including cost-benefit analyses, are needed before the medical community and governing bodies that regulate health-care systems will know how to best implement this technology. In the meantime, its judicious use should be based on the medical facts of each case, with careful consideration of the existing evidence and the available resources.

In the current context of expanding ECMO use and increasingly sophisticated technology, even in the absence of high-level evidence, it is important to anticipate and analyze the ethical dilemmas that will inevitably arise and to discuss potential approaches to resolving these complex clinical situations. In this article, we address some of these ethical issues—the use of ECPR, the bridge to nowhere, and the meaning of do not resuscitate (DNR) and CPR on ECMO—through the prism of real clinical scenarios and attempt to provide a framework to approach these dilemmas.

Case One: A 50-year-old man with no known past medical history arrives in the ED with unstable angina. Thirty minutes later he suffers a witnessed cardiac arrest with ventricular tachycardia noted at the outset. Despite 10 min of uninterrupted advanced cardiac life support, there is no return of spontaneous circulation. The attending physician calls a surgery consultation for consideration of ECMO.

To whom should ECPR be offered?

To answer the question of whether to offer ECPR, it is important to first address the role of conventional CPR in cardiac arrest. The use of CPR dates back to 1960. Since the 1970s, CPR has become the default resuscitation status in all cases of cardiac arrest, regardless of cause.[25,26] Although the decision to withhold CPR has been framed as an issue of patient autonomy,[27] others have argued that such decisions should be left to physicians to determine when CPR is futile.[28-30] Still others have suggested changing the default status of CPR when there is a very remote chance of benefit and near certain harm.[26] In such circumstances, a physician should recommend withholding CPR to protect the patient. Although disagreement remains regarding when it is appropriate to withhold CPR, a position advocating for the withholding of ECPR, when the likelihood of survival is remote, is even more compelling.

ECPR is a far more invasive and resource-intensive intervention than traditional CPR and has the capacity to prolong suffering considerably without changing the ultimate outcome.

Although the prognosis for survival with ECPR is uncertain during a cardiac arrest, the presence of multiple comorbid conditions, multisystem organ failure, devastating neurologic injury, or advanced age should all factor into the decision of whether to initiate ECPR.[7,19] ECMO requires an experienced multidisciplinary team, expensive equipment, and the use of an ICU bed, the availability of which may be limited. In centers that have the capability of initiating ECPR, there should be strict criteria for initiating and withholding this intervention. Criteria ought to reflect data from studies aimed at identifying factors that best predict outcomes from ECPR in different settings, thereby avoiding its use in patients unlikely to benefit.[7] If the use of ECPR becomes even more widespread, there is a real concern that it would be an expected intervention for patients suffering acute cardiac arrest. If this occurs, physicians would need to incorporate ECPR into advanced directive discussions, potentially requiring the development of a DNR with ECMO order.

Case Two: A 25-year-old woman who is a lung transplant candidate with advanced pulmonary hypertension is placed on invasive mechanical ventilation for hypoxemic respiratory failure with decompensated right-sided heart failure. To maintain her transplant candidacy, she is placed on venoarterial ECMO and subsequently extubated. Initially she does well with physical therapy and maintains her transplant candidacy. Over the following 2 weeks she develops renal failure requiring hemodialysis, becomes progressively deconditioned from limited participation in physical therapy, and is deactivated from the transplant list. However, she remains awake, alert, and conversant with her family and reports no discomfort from her supportive therapies. Attempts to wean ECMO support and maximize medical therapy result in respiratory and hemodynamic instability. She declines the option of endotracheal intubation or removal of ECMO.

What should be done with a patient on ECMO when there is no expectation for recovery or option for lung transplantation?

The decision to initiate ECMO as a bridge to transplantation is one that should include a thorough assessment of the ECMO recipient's transplant candidacy. Because there is no destination device therapy for respiratory failure, it is imperative to assess whether there are any contraindications to transplantation prior to ECMO initiation, so as to minimize the chance of creating a bridge to nowhere scenario. To that end, an absolute contraindication to ECMO is implementing it as a potential bridge to transplantation if transplantation will not be considered. Similar considerations should be made when initiating ECMO as bridge to recovery, adhering as closely as possible to accepted criteria; however, the prognosis for recovery is often uncertain, and decisions must be made based on the data available and provider expectations.

Despite physicians' best efforts to use ECMO only in those cases in which the chance of recovery or lung transplantation is reasonable, circumstances may arise that alter the prognosis and make these goals unattainable. When such situations occur, patients will find themselves unable to leave the ICU, dependent on ECMO with no alternative for life support—a bridge to nowhere scenario.

Because of the potential for ECMO dependence in an alert patient with no hope for recovery or transplant, ECMO may result in the ethical dilemma of a sentient patient in the ICU being kept alive with sophisticated and resource-intensive technology who has no chance of surviving to discharge. Although an established principle of medical ethics is that withholding and withdrawing life support are ethically comparable, this principle is not applicable when comparing an alert patient on ECMO with no other therapeutic options who declines removal of life support with a patient being denied ECMO for definitive medical reasons.

If a patient with respiratory failure presents without options for transplant or recovery, there would be no ethical issue in withholding ECMO. In view of the high resource burden of ECMO, it would be hard to justify using this technology to prolong a patient's life for days or weeks in the ICU with no hope of transplant or recovery. Patients in this condition who specifically requested ECMO might be upset by not receiving it; however, if appropriate medical justification is given demonstrating why ECMO would not achieve its intended goals, patients and families generally accept the medically and ethically justified decision, much as a patient who is unsuitable for transplantation would have to accept the decision of a transplant committee not to offer an organ because of compelling medical reasons. It is generally accepted that patient autonomy cannot dictate the use of each and every medical or surgical intervention that might offer minimal prolongation of a patient's life at great cost in human and material resources.

However, a decision to withdraw ECMO from an alert, objecting patient in whom it was appropriately initiated but for whom there is now no chance for recovery or transplantation is different from withholding ECMO from a patient for whom goals of ECMO cannot be realized. When a patient is begun on ECMO, the doctor-patient relationship evolves into a closer emotional and ethical bond than when a patient is being initially evaluated for ECMO. Once treatment begins,

patient trust and expectations of improvement in health increase. Patient autonomy becomes stronger in that situation compared with the case of a patient asking for a treatment that is not indicated. Patient autonomy would seem to warrant most deference in the immediate life-and-death situation of removing life support. It is inconceivable that an alert patient dying from cancer and reliant on a ventilator for life support would be disconnected from the ventilator against his or her wishes. The only reason to even consider removing ECMO from the objecting patient in case two, as opposed to the patient with cancer, is because of the much greater use of human and technologic resources. However, this cannot justify unilateral removal of life support.

Finally, and most importantly, it would be cruel to ignore the request of the patient to remain on ECMO and tell her that the device would be removed against her wishes. We and others believe that cruelty is unethical, and the patient would clearly suffer emotionally at the thought of impending death against her wishes (Baruch Brody, PhD, and Mark Siegler, MD, personal communications, July 10, 2013, and Art Caplan, PhD, personal communication, July 9, 2013). Such withdrawal would also certainly cause unacceptable emotional distress among both caregivers and family.

A patient who has capacity, as in the previously mentioned case, should first be given an opportunity to understand her medical circumstances and the anticipated outcomes. If the patient chooses not to have ECMO withdrawn, her decision should be respected based on the ethical principles outlined previously, even when there are serious issues of resource utilization. Although the bridge to nowhere scenario is not unique to ECMO, it is a particularly challenging dilemma when using this advanced form of life support in patients with preserved capacity.

When a patient lacks capacity and her wishes regarding end-of-life care are unknown, the decision regarding the continuation of life support with ECMO rests with the patient's surrogate decision-maker and her physicians. In such cases, the patient's physicians should meet with the surrogate and communicate as accurately as possible what the prognosis and options are, seek his or her understanding, and help reach a decision together regarding what is perceived to be in the patient's best interests. There is no moral dilemma or ethical ambiguity when the surrogate and physician agree on withdrawal of ECMO, paralleling the rationale for withholding ECMO therapy.

However, there are ethical reasons to distinguish between withdrawal of ECMO against the wishes of a sentient patient and, when a patient is not alert, withdrawal against the wishes of a surrogate. The primary ethical obligation of a physician is to his or her patient and not to surrogates. In a situation in which a resource-intensive technology is merely prolonging the dying process rather than accomplishing any therapeutic goal for the patient, a strong case can be made to discontinue the intervention, with appropriate concessions of timing to the surrogates. There is no issue of emotional or physical patient suffering in that case and it is even possible, if not probable, that the patient would not want his or her life prolonged in such circumstances. This is a situation that could reasonably be called one of medical futility, in that the goals for which ECMO was initiated cannot be achieved, and this resource-intensive technology is prolonging the dying process.

Ethical justification and legal protection have been granted to physicians who withdraw life-sustaining treatment over objection in the State of Texas as long as certain procedures have been carried out.[31] The Guidelines on Institutional Policies on the Determination of Medically Inappropriate Interventions, which served as a basis for the medical futility component of the Texas Advanced Directives Act of 1999, justifies the withdrawal of life-sustaining therapy against the wishes of the surrogate on the grounds of respect for "the moral value of physician and institutional integrity in discerning the limits of medical interventions," which "complements the right of patient determination that must be given both voice and effect in any forum for medical decision making," and is "rooted in a combination of concerns such as avoiding harm to patients, avoiding provision of unseemly care, and just allocation and good stewardship of medical resources."[32,33] The determination of medical inappropriateness is left to the judgment of the medical profession, so long as there is agreement by an appropriate institutional review. Although these guidelines specify "patient (or surrogate decision-maker)," Baruch Brody, PhD, former director of the Center for Medical Ethics and Health Policy at Baylor College of Medicine, and coauthor of these guidelines, is unaware of any case that used the Texas Advanced Directives Act to remove life support in a futility situation against the wishes of a patient with capacity, although he could not vouch for cases at other centers (Baruch Brody, PhD, personal communication, July 10, 2013).

Although legal application of these guidelines is limited to Texas, the ethical justification that forms their basis can be universally applied and is particularly applicable to the ECMO bridge to nowhere scenario. Whether, however, physicians would invoke medical futility as a reason for removing ECMO against the wishes of surrogates in states other than Texas without legal protection is questionable and would depend on local policies and practices referable to that area.

To facilitate decision-making and optimize end-of-life care, every effort should be made to proactively inform patients and their families of possible outcomes prior to initiating ECMO (e-Appendix 1). In addition to obtaining consent for the implantation of the device,

attention should be paid to prognosis, complications of ongoing device therapy, and the possibility that the anticipated result (recovery or transplantation) might not be achieved. Introducing the concept of a bridge to nowhere up front can help prepare the patient and his or her family for this possibility and define circumstances in which withdrawal of life support would be medically and ethically appropriate.[34] Although no amount of discussion can fully prepare a patient for the feeling of being permanently confined to an ICU while receiving life-sustaining ECMO support, the greater the effort given to obtaining informed consent before ECMO, the easier it may be to reach a consensus on withdrawal later if ECMO is no longer achieving its intended goals.[35] The Extracorporeal Life Support Statement of Purpose (e-Appendix 1) is meant to enhance informed patient consent by clearly stating the goals of ECMO and the consequences of not achieving them. The document is not legally binding, but we have found it helpful in alerting patients and families that there is a possibility that ECMO may have to be withdrawn, thereby preparing them emotionally for this unfortunate outcome.

When obtaining informed consent for ECMO, it is important to explain that if the goals of ECMO cannot be achieved, death will result from superimposed illnesses or complications related to the device. Of utmost importance is the need to assure the patient and family that comfort will be maintained throughout the patient's course. The role of palliative care services in patients on ECMO has yet to be defined and is an area that requires study. Given the anticipated level of emotional and existential distress in such scenarios, it is reasonable to involve palliative care early in such cases.[36] Finally, the withdrawal of ECMO and other life-sustaining therapies remains subject to the laws and policies governing local institutional practices.

Case Three: A 45-year-old man on venoarterial ECMO for end-stage congestive heart failure as a bridge to decision develops profound septic shock and multiorgan failure. Despite maximizing the extracorporeal blood flow rate, he has increasing vasopressor requirements. He is no longer a candidate for transplantation and is not expected to survive. He had previously requested to be "full code"; however, his physicians believe that CPR would be futile given his underlying heart disease and superimposed irreversible multiorgan failure.

What is the meaning of DNR and CPR when venoarterial ECMO is in place?

In the case of venoarterial ECMO, where the device is providing both respiratory and circulatory support, some degree of cardiopulmonary resuscitation is effectively ongoing. In some circumstances, as evidenced by success with ECPR, ECMO may be able to provide sufficient cardiopulmonary support to avoid death in the setting of cardiac arrest.[6,7,20] In other cases, where ECMO is providing only partial support, cardiac arrest would likely result in death if additional resuscitative efforts were not provided, in which case a DNR order still has significance. Because it may not be possible to distinguish between these scenarios prior to the onset of cardiac arrest, code status should be addressed with all ECMO patients and readdressed as clinical circumstances change, similar to the approach with any critically ill patient. The determination of code status should be based on the medical facts of the case in conjunction with the patient's preferences, rather than solely based on the level of support provided by ECMO. Every effort should be made to avoid CPR when it is deemed to have a remote likelihood of success, similar to the withholding of any futile medical therapy. In cases where there remains a reasonable chance of recovery or transplantation despite cardiac arrest, CPR may be an appropriate intervention. If it can be determined that ECMO is supporting cardiopulmonary function to such a degree that cardiac arrest would not lead to death, the focus of the discussion regarding goals of care should shift. The focal point for discussion should no longer be cardiac arrest, per se, but rather the point at which recovery is deemed extremely unlikely, or the patient's goals can no longer be met. This may be signaled by irreversible multiorgan failure.

Limiting ECMO Support

The vignettes in this article illustrate the goal of ECMO to bridge patients either to recovery or transplant. However, they also highlight the inherent limitations of device-based therapies. When ECMO is no longer meeting its intended goals, a discussion of limiting treatment to either no escalation of life support or withdrawal of life support should be considered. Although the amount of ECMO support may be easily adjusted at the bedside, increases in ECMO blood flow, CO_2 removal, or oxygen delivery are akin to increases in vasopressor doses or the fraction of oxygen delivered through the ventilator. No further escalation of ECMO support—including not replacing a failing ECMO component—may be a reasonable option to offer under such circumstances. Limiting life-sustaining treatments may also consist of withholding vasopressors in the face of worsening vasodilatory shock that could not be supported with ECMO alone. If the patient is alert and willing, he or she should participate in these decisions. If a decision is made to limit extracorporeal support, a DNR order must be obtained.

Conclusions

As the use of ECMO continues to grow, clinicians will increasingly confront complex and sensitive ethical issues. It is important that the wisdom with which

ECMO is used keep pace with advances in its use. For patients and their surrogates to be adequately prepared to make informed medical decisions, it is the physician's responsibility to disclose not only the possibilities but also the limitations of these medical technologies. Our obligation to respect the autonomy of the patient and work toward a common goal is unchanged by the addition of a new device. A discussion of the meaning and nature of CPR and DNR and the possibility of an ECMO-created bridge to nowhere is essential. As cardiac arrest is the final common pathway before circulatory death, ECPR should be used when there is reasonable expectation of benefiting the patient and not as a routine intervention in every instance of cardiac arrest.

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Additional information: The e-Appendix can be found in the "Supplemental Materials" area of the online article.

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