Neither Ethical nor Prudent

Why Not to Choose Normothermic Regional Perfusion

by ADAM OMELIANCHUK, ALEXANDER MORGAN CAPRON, LAINIE FRIEDMAN ROSS, ARTHUR R. DERSE, JAMES L. BERNAT, and DAVID MAGNUS

In transplant medicine, normothermic regional perfusion (NRP) can be used to increase the number of high-quality organs procured and to make organ allocation more efficient. Yet NRP faces ethical and legal challenges because it restores the donor's circulation, thus invalidating a death declaration based on the permanent cessation of circulation. Tortuous and inaccurate arguments are used to justify NRP. *Ethical parsimony* favors an alternative that yields comparable outcomes: normothermic machine perfusion.

The practice of obtaining organs from patients who die after life-sustaining treatment has been withdrawn generated ethical debate when it was initiated by the University of Pittsburgh Medical Center three decades ago.[1] The concern was that the "Pittsburgh protocol" violated the dead donor rule (DDR), which holds that vital organs may be procured only from patients who are dead and that physicians may not cause death while or for the purpose of procuring vital organs.[2] In time, a consensus emerged among transplant programs and health authorities around the world that the practice, now known as "donation after circulatory determination of death"[3] (or "DCDD"), is consistent with ethical norms and legal requirements because permanent cessation of the donor's circulation means that death has occurred.[4] Today, DCDD supplies a substantial percentage of deceased-donor organs in many countries including the United States, where it provided more than a third of all organs from deceased donors in 2023.[5]

Unfortunately, DCDD organs suffer warm ischemic damage after life-sustaining technologies are removed and the donor is allowed to die. The customary method for reducing such damage is rapid cooling of the body's core, removal of the organs that will be transplanted, and their placement in static cold storage to preserve them temporarily. Organs can be maintained for only a limited time because prolonged cold storage increases the risk of graft dysfunction and complications for the recipient.[6]

Adam Omelianchuk, Alexander Morgan Capron, Lainie Friedman Ross, Arthur R. Derse, James L. Bernat, and David Magnus, "Neither Ethical nor Prudent: Why Not to Choose Normothermic Regional Perfusion," *Hastings Center Report* 54, no. 4 (2024): 14-23. DOI: 10.1002/hast.1584

One strategy to extend the preservation period, which has recently come to be used in DCDD, is to perfuse transplantable organs with warm oxygenated blood or perfusate.[7]

Normothermic regional perfusion (NRP) is one such strategy that reverses some of the effects of ischemic damage, something that static cold storage cannot do.[8] In NRP, an extracorporeal membrane oxygenation (ECMO) machine circulates oxygenated blood to the organs to be transplanted, and arteries that carry blood to the brain are occluded. When only the liver, kidneys, and pancreas are recovered, the procedure is known as "A-NRP" because circulation is clamped off above the abdominal region; when the heart or lungs are also obtained, the procedure is termed "TA-NRP" because blood flows into all organs in the thoracoabdominal space, which restores cardiac function, and is occluded at the aortic arch.

NRP was first used in 1997 and subsequently incorporated into the DCDD protocols of some medical centers in the United Kingdom and Spain.[9] As those programs reported improved results over conventional DCDD, some transplant programs in the United States started performing A-NRP and TA-NRP. In 2021, the American College of Physicians urged U.S. medical centers to pause before implementing such protocols to allow further study. This professional organization, which termed NRP with DCDD "a protocol more accurately described as organ retrieval after cardiopulmonary arrest and the induction of brain death,"[10] was not alone in concluding that NRP does not meet existing ethical or legal standards.[11] In response, proponents argue that NRP improves graft survival rates and surgical efficiency, increases the number of organs procured, and reduces overall costs.[12] Some proponents further argue that it is ethical and aligned with the current law,[13] while others recommend a change in the law to treat the permanent loss of circulation as a proxy for the permanent loss of brain function.[14] These claims have been cross-examined not only on ethical and policy grounds but also on scientific grounds that have, for example, led transplant programs in the United Kingdom to suspend the use of TA-NRP while important issues are investigated.[15] In short, NRP faces three major objections, one that alleges a failure of legal compliance, one that claims the dead donor rule is violated, and one from the failure to respect persons and their autonomous choices.

Recognizing the importance of these issues, the American Society of Transplant Surgeons (ASTS) communicated in a recent consensus statement that "[t]o preserve public trust in organ donation, ethical issues need to be investigated, navigated, and discussed but are not insurmountable. NRP must be conducted within the confines of the UDDA. Finally, communication with donor families is paramount to ensure transparency."[16] While the ASTS is optimistic that NRP will come to be accepted, it recognizes the need to establish a "wider national consensus on the ethical and legal acceptability of NRP."[17] Claiming to be "fully cognizant of ethical concerns raised regarding NRP," the ASTS nevertheless supports its "ongoing utilization" and is confident that it "does not violate essential moral, philosophical, and bioethical medical precepts."[18] In recommending that NRP be implemented now, based on the promise that an ethical and legal consensus will emerge in its favor in the future, the ASTS views critics as pessimists who hesitate to authorize a lifesaving therapy. To policy-makers and administrators, their statement communicates that proceeding with NRP is presumptively ethical because it appears to promote clinical utility, helps donors donate effectively, and will, like the Pittsburgh protocol, come to be accepted.

Yet the ethical and legal issues are harder to resolve than NRP proponents would have people believe. We argue that the restoration of circulation in NRP invalidates the declaration of death, and we explain why arguments to the contrary are unconvincing. The effort to wedge NRP into existing ethical frameworks poses significant risks to public trust in organ donation, which is further undermined by recommendations from the ASTS and other NRP proponents about the limited medical information that needs to be disclosed when obtaining consent.

Under the law, what matters in making a circulatory determination of death is *whether* circulation is present in the individual's body, not *why* it is there, and whether circulation has *permanently* ceased.

We believe that there is no need to take such an unwise step and proceed with NRP on such a weak basis because an alternative means of oxygenated perfusion, normothermic mechanical perfusion (NMP), can be performed *ex situ* by connecting organs to a machine after they have been removed from the donor. As we discuss below, both NMP and NRP seek the same objectives: to salvage some deceased donor organs that might otherwise not be usable, to improve the quality of other organs, and to reduce waste and improve equity by providing more time for organ allocation. We conclude by showing that when choosing between alternative means of achieving these results, prudent U.S. policy-makers, physicians, and transplant centers should prefer the ethically simpler

one rather than the one that depends on performing verbal gymnastics and misreading statutes or that generates ethical controversies that may undermine public trust in organ donation.

Irreversibility, Permanence, and the Restoration of Circulation

There is a strong case that NRP does not comply with the legal criteria for determining death. With minor variations, all U.S. jurisdictions recognize the two standards for determining death found in the Uniform Determination of Death Act (UDDA): "An individual who has sustained either (1) irreversible cessation of circulatory and respiratory functions, or (2) irreversible cessation of all functions of the entire brain, including the brain stem, is dead. A determination of death must be made in accordance with accepted medical standards."[19]

When DCDD was first proposed, critics argued that DCDD donors are not dead under the circulatory-respiratory standard because resuscitative measures could restore donors' circulation and respiration, meaning the cessation of these functions is not "irreversible" at the moment when they are declared dead. DCDD came to be accepted, however, on the understanding that what the statute—like the common-law standard based on "a total stoppage of the circulation"[20]—actually requires is that the cessation of functions remain unchanged in perpetuity. The UDDA expresses this requirement as "irreversible cessation" to remind physicians of the need to rule out confounding conditions that could be masking relevant signs of life in certain circumstances. In this context, "irreversible" was intended to be a checkpoint in the process of determining whether the loss of function is permanent. But in the ordinary practice of medicine, outside the context of organ donation, when hospitalized patients with a do-not-attempt-resuscitation (DNAR) order experience cardiorespiratory arrest, physicians routinely declare death even though the cessation of circulation and respiration might in some cases be reversed. The report that the medical consultants to the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research prepared on the diagnosis of death explained "irreversible" as follows: "*Irreversibility* is recognized by the persistent cessation of functions during an appropriate period of observation and/or trial of therapy. In clinical situations where death is expected, where the course has been gradual, and where irregular agonal respiration or heartbeat finally ceases, the period of observation following the cessation may be only the few minutes required to complete the examination. Similarly, if resuscitation is not undertaken and ventricular fibrillation and standstill develop in a monitored patient, the required period of observation thereafter may be as short as a few minutes."[21] Thus, the circulatory criterion of death is satisfied when a person's circulation has ceased permanently.[22]

Of course, were respiration and circulation to resume spontaneously, a prior determination of death would be invalidated. Therefore, the typical DCDD protocol allows death to be declared only when asystole continues during a "no touch" period of at least five minutes, which is long enough to rule out autoresuscitation. Since DCDD involves patients (or their surrogates) who have rejected all attempts to reverse the loss of circulation and respiration following the removal of life-sustaining treatment, the loss of these functions will be permanent.

With NRP, however, circulation is restored through a vascular circuit that supplies oxygen and nutrients to, and removes waste from, the donor's organs and tissues, thereby contradicting the premise on which death was declared, namely, that circulatory functions have permanently ceased. Indeed, in TA-NRP, both blood flow and cardiac function resume, which proponents of NRP argue has the additional benefit of making possible "functional assessment" of the heart, which is informative for transplant surgeons.[23] With the determination of death invalidated, however, procuring organs from donors through NRP violates the DDR, since such donors are not dead and the removal of vital organs would cause their death, thus risking a homicide charge. Notably, Australia does not permit the use of NRP.[24]

Unconvincing Defenses

In response to this straightforward conclusion, those in favor of NRP argue that its use is consistent with death-determination statutes because the circulation that NRP restores in DCDD donors should not be equated with the circulatory functions in the statutory definition of death. At the center of several interconnected arguments is the semantic claim that NRP does not "restore circulation" but merely "perfuses tissues *in situ*."[25] These arguments hold that "restoring circulation" mischaracterizes what this use of ECMO does because that language implies reviving the patient, which is not the objective of NRP; instead, the procedure merely aims at "[r]estoring the circulatory function of the heart"[26] or "[p]erfusing the thoracic and abdominal organs."[27] But this distinction misstates the relationship: circulation, whether generated naturally or artificially, exists for the purpose of perfusing organs and tissues, and the permanent loss of circulation brings about death because, without oxygen, organs lose the ability to function.

NRP proponents raise two other, related objections. First, they argue that, since "resuscitation" involves a therapeutic intent that NRP lacks, NRP's use of ECMO must be interpreted as an act of "reperfusion," which "does not change the circumstances that lead the family, in collaboration with the care team, to conclude that the possibility of a meaningful life no longer exists for the patient."[28] The problems with

these arguments go beyond the complex web of words the proponents spin, as they try to separate perfusion from circulation or to distinguish restoration of circulation from resuscitation of the patient. The central weakness is that they read concepts into the death-determination statutes that aren't there. The UDDA and comparable laws say nothing about resuscitation. The statute describes a civil status—being dead—which occurs because of certain characteristics of an individual; in the case of DCDD, the relevant one is the permanent cessation of circulatory and respiratory functions. Likewise, the presence or absence of a therapeutic intent is irrelevant. Under the law, what matters in making a circulatory determination of death is *whether* circulation is present in the individual's body, not *why* it is there, and whether circulation has *permanently* ceased.[29]

NRP proponents try to rewrite the death-determination statutes in another way when they assert that "irreversible cessation of circulatory and respiratory functions" refers only to the loss of "spontaneous cardiorespiratory function."[30] This claim would extend the UDDA to patients who are placed on ECMO during surgery. Such patients lack spontaneous cardiac activity but, of course, are not regarded as dead on the basis that their circulation occurs artificially rather than spontaneously. Moreover, even were the spontaneity of circulation a criterion under the UDDA—which it is not—the TA-NRP protocol results in "reperfusion of the heart and coronary circulation, which enables resumption of spontaneous cardiac activity" and thereby "restores blood flow independent of the extracorporeal circuit."[31]

The proponents' second objection to the conclusion that the restoration of circulation invalidates a DCDD death determination is that "NRP cannot resuscitate the deceased because the capacity for spontaneous function remains absent and because interventions [to restore it] were determined medically ineffective in accordance with accepted medical standards."[32] The claim that the "capacity" for spontaneous function is absent in DCDD donors is false since many patients who have just been declared dead under the circulatory standard still possess the capacity for spontaneous circulation. As just noted, TA-NRP typically results in resumption of spontaneous cardiac activity, which is not surprising given what happens in other cases of cardiopulmonary arrest where cardiopulmonary resuscitation (CPR) produces a return of cardiac function. Likewise, if CPR delivers blood to the brain in sufficient quantity, normal functions can sometimes be restored even when resuscitation commences more than five minutes after a sudden cardiac arrest. Interventions that could achieve such results are withheld in DCDD not because they would be "medically ineffective" in restoring circulation but because the family and medical team have concluded that the patient does not want such an attempt to extend life or would not benefit from it.

Calling the interventions in the donor "medically ineffective" in achieving spontaneous cardiac function equivocates between "physiologically ineffective" and "medically inappropriate." The first reading must be rejected for several reasons. Most basically, ECMO *is* effective in producing the circulation needed to achieve regional perfusion. Further, if ECMO were physiologically ineffective in establishing circulation, NRP practitioners would not occlude vessels to the brain to prevent brain perfusion and the possible restoration of neurological functioning. Thus, the proponents apparently mean that one must conclude that ECMO is "perfusing" the body because it would be "medically inappropriate" to provide "circulation," as the patient or family rejected any attempts at resuscitation—the epitome of begging the question.

In short, the proponents' arguments are convoluted, factually inaccurate, and twisted by attempts to introduce concepts such as *therapeutic intent*, *spontaneous function*, and *medical ineffectiveness* into a statute where they neither appear nor belong. The arguments fail to refute the conclusion that the circulation restored by NRP in the body of a DCDD donor necessarily negates the premise—that circulation will not return—on which the legal determination of death was based.

Physicians who recommend not disclosing information about NRP that might alarm or confuse donor families want to avoid choices that fail to maximize benefits to the transplant enterprise.

The Risk of Unintended Consequences

Ultimately, proponents do not rest their case on a convincing rebuttal to the critiques. Instead, they contend that NRP will allow transplant programs to maximize the lifesaving impact of DCDD by improving the number and quality of transplantable organs through the efficient use of financial and medical resources.[33] Yet that is an incomplete description of the problem because the problem calls for a solution that safeguards public trust and is consistent with the DDR.

While the organ shortage is serious, and creative ways to meet it are needed, embracing NRP based on such weak arguments substantially risks undermining public trust.[34]

The willingness to be a deceased donor rests on people's confidence that they will have died before organs are removed.[35] Americans' conceptions of death vary, ranging from the belief that death occurs as soon as someone ceases to be aware of the world to the view that life continues as long as there is breath, even when that is provided by a ventilator, to the belief that a person is in a transitional state but not dead for a time after they cease breathing. The neurological criteria for determining death are poorly understood, and doubts about whether they define "biological death" have led some to suggest that a revised UDDA should allow anyone who objects to "brain death" to reject the use of that standard to declare them dead.[36] This social trend speaks against one possible solution some NRP proponents favor: grounding the law on a brain-based standard for determining death, under which only perfusion of the brain, rather than systemic circulation, would need to have ceased permanently for a death determination to be valid.[37] But even if such a change were made, a serious diagnostic problem needs to be resolved, namely, that insufficient evidence exists that brain circulation has completely ceased when TA-NRP is used.[38] More significantly, given the public's greater skepticism about "brain death," shifting the basis for declaring death in DCDD from circulatory to neurological functions without public endorsement risks reducing the number of people willing to become donors after the withdrawal of life support.

However these issues are to be resolved, the public expects physicians to put patients' interests above the interests of others and to treat every person as an end and never solely as a means. Since physicians would violate these ethical imperatives if they were to declare the death of potential donors while also caring for patients who might receive organs from these donors, U.S. law forbids physicians from playing both roles.[39] Yet if the physicians who determine death in DCDD and organ procurement organizations that verify such deaths know that these donors' circulatory functions will be restored by NRP in order to benefit organ recipients, these physicians represent the sort of conflict of interest that the law and medical ethics prohibit, particularly regarding the procurement team's efforts to cut off blood flow to the donor's brain so as to ensure an unverified form of brain death. This could lead members of the public to conclude that donor hospitals, organ procurement organizations, and transplant programs value organ recipients' welfare over donors'. The resulting loss of public confidence could reduce the number of organs available for transplantation. At the very least, candor is needed regarding what is happening and why since the public has an interest in knowing that there is a controversy about whether NRP protocols are consistent with the DDR.

The Ethical Unacceptability of Obfuscation and Withholding Information

Given the interest that anyone would have in being correctly diagnosed as dead before their vital organs are procured, one would expect NRP proponents to strongly recommend full disclosure about NRP to potential donors and their families. Instead, proponents' writings reveal hesitancy to disclose facts about NRP. For example, they have warned against "dumping all details on grieving traumatized families," and they advise further study about whether families "want to know, or need to know, specific NRP techniques" since withholding "technique details" is standard practice in obtaining valid authorization under DCDD protocols.[40] But this reasoning targets a strawman. It is never good practice to ignore grief and trauma when choosing how to communicate, much less to "dump all details" on patients and their families. More importantly, the term "technique details" fails to accurately describe the morally relevant facts about NRP, which include that it restores circulation in the donor's body, requires active steps to prevent blood flow to the brain, and fails to employ tests to determine whether blood reaches the brain or whether its functions, including perception of pain or minimal consciousness, have been permanently lost.[41]

Hesitation to disclose relevant information is apparent in the euphemistic—and, indeed, obfuscatory—recommendations of the ASTS: "Terminology such as 'reanimation,' 'resuscitation,' and 'ECMO' should be avoided when discussing NRP as these terms do not clearly reflect the process of organ recovery from a donor who has already been declared deceased due to hemodynamic arrest. In lieu, more specific and less emotionally laden terms such as 'in situ tissue perfusion' or 'dynamic in situ organ assessment' should be used."[42] This recommendation presents three problems. First, the meaning of "hemodynamic arrest" does not align with the statutory requirement of permanent cessation of circulatory functions. Second, while a desire to avoid terms such as "reanimation" and "resuscitation" is understandable, avoiding them is problematic precisely because the activities they name are recognizably linked to restoring circulation. Third, clarity is supplanted by Latinate jargon when "ECMO" is omitted in describing the means used and "in situ tissue perfusion" or "dynamic in situ organ assessment" is presented as the end being sought. The ASTS recommendations thus disregard the basic ethical principle of respect for persons, which requires clear and comprehensible communication of the information that would matter to a decision-maker. The information might upset families because they had been told that interventions to restore circulation will be forgone since they would not benefit the patient, yet the families can see that ECMO restores circulation, in violation of the DNAR order that was supposed to allow their loved one

a peaceful passing. Withholding the information—and replacing it with medical mumbo jumbo—is deceptive. Indeed, the use of euphemisms and jargon to steer families' thinking and to keep them from making what the physician thinks would be the wrong decision resembles medical paternalism, which was an early target of bioethics, except that paternalists hoped to keep patients from making choices that they thought were not in the patients' best interests, while physicians who recommend not disclosing information about NRP that might alarm or confuse donor families want to avoid choices that fail to maximize benefits to the transplant enterprise.

Evaluating Alternatives to NRP

Must such concerns about the legality, ethics, and public acceptance of NRP be swept aside because of the benefits that postmortem perfusion of organs offers for treating more patients awaiting a transplant? Not necessarily, since normothermic machine perfusion (NMP) offers an alternative means of achieving comparable benefits.[43] This machine perfusion is performed on organs removed from deceased donors and thus leaves undisturbed the permanent cessation of circulation in the donor's body.

The technology and techniques of NMP are still evolving but show promise.[44] For example, one multi-institutional randomized controlled trial had positive outcomes when NMP was used in transplanted hearts. Eighty-nine percent of the DCDD hearts that underwent machine perfusion were transplanted and produced six- and twelve-month patient and graft survival rates that were not inferior to those of the control group, who received hearts from donors declared dead based on neurological criteria,[45] the source that has long been considered the "gold standard" for heart transplants.[46] Another recent study directly compared NRP to NMP in liver transplantation. It found that NMP succeeded 85 percent of the time (34/40), which was 15 percent higher than the 70 percent rate when NRP was used (157/224).[47] TA-NRP facilitates procuring more organs from a donor (specifically, both liver and heart); NMP usually allows for only one or the other, although it may benefit combined heart-liver transplants.[48]

Nonetheless, TA-NRP provides a superior opportunity for functional assessment of hearts in situ and permits the circulation of the body's metabolic substrates, which does not occur with NMP. In sum, while NMP allows for prolonged perfusion after extraction, which can buy extra time for liver graft assessment and repair,[49] its medical benefits may not yet quite equal those of NRP, although they may increase as a result of further research on perfusates and biomarkers.[50]

Proponents of in situ perfusion, particularly those focused on obtaining hearts, argue that, since TA-NRP is less expensive and resource intensive than NMP, it can be adopted faster and more equitably than NMP. The estimated costs of NMP appear to be higher than those of NRP because NMP requires the purchase and maintenance of a purpose-built machine, whereas NRP uses already purchased ECMO machines and NMP relies more on disposable supplies.[51] The argument from material costs is not very compelling, however, since transplant specialists view NMP not as a competing technology but, rather, as a complementary means of oxygenated perfusion that can support and rehabilitate organs regardless of whether procurement involved TA-NRP, A-NRP, or the standard protocol after brain death.[52] Moreover, the added expenses of NMP are only a small fraction of the total cost of a transplant (the average charge for a heart transplant in 2020 was $1,664,800[53]), which is still a cost-effective alternative to paying for ongoing care of patients with organ failure and which also produces substantial social and economic benefits by restoring recipients to productive work and family life, among other benefits.[54]

No linguistic hoops need to be jumped through to align normothermic machine perfusion with the dead donor rule or the statutory standards for determining death.

Nor can one be certain that NRP will bring an overall benefit to DCDD more quickly or extensively than NMP could. TA-NRP may not be widely implemented while research about the extent and effects of brain perfusion under current NRP protocols is being completed,[55] the applicability of homicide laws is being resolved,[56] and the public is being honestly informed about what NRP entails and reaching conclusions about the ethics of the procedure. Although the Organ Procurement and Transplantation Network (OPTN) Ethics Committee "shares the enthusiasm of the transplant community in developing and implementing solutions to improve the transplant system and reduce wait times and deaths for patients awaiting organ transplantation,"[57] it found that NRP raises "serious ethical concerns"[58] and concluded that, "[a]s with all new technologies, consideration for how the technology can be implemented ethically is critical to its widespread adoption and acceptance by the public."[59]

Applying Ethical Parsimony to NRP

The decision to implement an NRP protocol turns on more

than whether it is cheaper or more efficient than NMP at improving the quality of deceased-donor organs and even salvaging some that would otherwise be discarded and at extending preservation times, which can facilitate more just and well-ordered allocation of organs. These laudable goals are incomplete unless another is included: acting in a way that is clearly consistent with the law and accepted medical ethics. Those who speak for the ASTS believe that NRP probably meets these goals and recommend that the procedure be incorporated into DCDD, even while its ethicality and legality continue to be explored. They concede, however, that a broader consensus is needed to implement NRP more widely.

Among other things, the OPTN has advised its members that they need to resolve questions about whether NRP adheres to the DDR and whether the risks of nonmaleficence (harm to public trust, distress to clinicians) are adequately minimized.[60] For transplant professionals and programs that are undecided—including those that believe that NRP might be ethically justifiable—a good reason exists *not* to implement NRP, based on a prudential rule, which we term "ethical parsimony," that is derived from Occam's razor. That ancient philosophical precept favors theories that postulate "fewer entities, processes, changes, or explanatory principles"[61] that complicate proving (or disproving) the theory and introduce both potential sources of error and barriers to comprehension. Similarly, ethical parsimony holds that, in the choice between competing means of achieving a result, the ethically simpler one is to be preferred. Ethical parsimony favors policies and actions that depend upon fewer (controversial) justifications, procedural requirements, semantic changes, or subjective judgments about which good outweighs another. The more complex an ethical analysis is, the more vulnerable it is to objection, misinterpretation, and miscommunication. By contrast, the simpler the analysis, the less there is to dispute, distort, or misunderstand. If option A requires a simpler analysis than option B to fit within a widely accepted ethical framework, then A is the better choice.

This kind of prudential reasoning is not without precedent. In 1998, scientists opened up new but controversial avenues for biomedical research and potential therapies when they succeeded in creating embryonic stem cell (ESC) lines from human blastocysts donated from in vitro fertilization clinics.[62] Although the Clinton administration set up a program in 2000 to fund research using human ESCs, the following year, President Bush sparked a heated public debate when he suspended that program. Six years later, the debate cooled when research in somatic cell differentiation produced induced pluripotent stem cells (iPSCs),[63] which could be used in place of ESCs. Although the equivalence of iPSCs to ESCs was initially disputed,[64] researchers largely agreed that the ethical concerns surrounding ESC could be circumvented because iPSCs offered comparable benefits without destruction of human embryos. Therefore, special legislation was not required to authorize federal funding for the creation of iPSCs, nor did researchers need to obtain parental consent for embryo use and gamete donation to create new cell lines.[65] None of this is to say that the use of human embryos could not be justified. The point is that the ability to conduct studies with iPSCs obviated the need for ESCs and thereby avoided the ethical controversies and complex arguments that were invoked to justify using ESCs. The human stem cell research saga thus confirms the value of ethical parsimony: if goals can reasonably be achieved by an option that is simple and uncontroversial, then, as a matter of prudence, one should choose it over other options that require complex or convoluted justifications and generate strong disagreement.

Applying this prudential approach to the procurement of DCDD organs clearly means implementing NMP over NRP. No linguistic hoops need to be jumped through to align NMP with the DDR or the statutory standards for determining death. No ad hoc process of tendentiously rewriting the statutory requirements for determining death need occur. No investigation need be undertaken into whether patients and their family members want euphemisms and evasions rather than clear explanations about what procedures will be performed after death is declared and what effects they will produce.

Indeed, some NRP proponents understand this and have recommended the following: "[NMP] is less ethically complex than NRP, so its use is encouraged as the primary method for heart procurement in [DCDD]."[66] We concur with this recommendation and hope that its implication—that prudence favors the simpler, less contentious course—is recognized by every institution deciding whether to employ NRP.

Ethical parsimony may even favor continuing with static cold storage, the current method of preserving organs for transplantation, if an institution cannot yet provide NMP for DCDD organs. While static cold storage may not increase the number of organs for transplant as efficiently as NRP does, it does not risk decreasing donations should NRP create public mistrust as a departure from the DDR and a risk to donor safety. In contrast, static cold storage clearly complies with the legal standard for circulatory determination of death and the ethical standards regarding disclosure and permission for deceased organ donation. Nonetheless, when NMP is available, it should be favored over static cold storage because it improves the number of transplantable organs, reduces waste, and extends the period available for orderly allocation and distribution of organs while also being fully consistent with existing law and generally accepted medical ethics.

The Wise Choice: NMP, not NRP

There are good reasons to reject NRP, as it fails to satisfy legal standards, comply with the dead donor rule, and inspire confidence in the disclosure process with donors and their decision-makers. Even those who hold the opposing view recognize that the use of NRP does not enjoy anything close to a consensus in the medical profession. Unless the law changes, informed consent processes are implemented, and the public comes to accept NRP, DCDD programs seeking to increase the benefits of postmortem organ perfusion should adopt NMP and forgo NRP.

Programs using NMP have demonstrated that it increases the number and quality of organs procured from DCDD donors while also respecting core ethical principles of clinical care, including physicians' obligation to fully inform patients and their authorized decision-makers about what they propose to do, and honoring the letter and spirit of the law, as encapsulated in the DDR. Ethics committees at hospitals and transplant programs that view NRP through the lens of ethical parsimony will see how imprudent it would be to approve an ethically contested method of organ procurement when NMP can produce comparable results without the logical and linguistic complexity entailed in arguments for NRP and the ethical and legal controversies that it raises, all of which endanger public trust in organ donation.

Disclosure

Lainie Friedman Ross participated in writing the statement from the OPTN Ethics Committee.

Acknowledgment

We are grateful for the feedback given on an earlier draft of this paper by the faculty of the Center for Medical Ethics and Health Policy at Baylor College of Medicine.

Notes

1. M. A. DeVita and J. V. Snyder, "Development of the University of Pittsburgh Medical Center Policy for the Care of Terminally Ill Patients Who May Become Organ Donors after Death following the Removal of Life Support," *Kennedy Institute of Ethics Journal* 3, no. 2 (1993): 131-43.

2. J. Lynn, "Are the Patients Who Become Organ Donors under the Pittsburgh Protocol for 'Non-Heart-Beating Donors' Really Dead?," *Kennedy Institute of Ethics Journal* 3, no. 2 (1993): 167-78; A. L. Dalle Ave, D. P. Sulmasy, and J. L. Bernat, "The Ethical Obligation of the Dead Donor Rule," *Medicine, Health Care, and Philosophy* 23, no. 1 (2020): 43-50.

3. "Donation after circulatory determination of death" is sometimes abbreviated as "DCD," which is confusing because "DCD" was previously used for "donation after cardiac death" and "donation after circulatory death" and because those phrases suggest that the absence of cardiac activity or circulatory and respiratory functions is "death" rather than the means by which death is determined. When the withdrawal of life-sustaining treatment is planned, the procedure is called "controlled DCDD"; the "uncontrolled" version, which is practiced in about half of the countries in Europe but not in the United States, involves donors who experienced a sudden cardiopulmonary arrest in or outside a hospital when either they could not be resuscitated or no attempt to resuscitate them was made.

4. J. L. Bernat et al., "The Circulatory-Respiratory Determination of Death in Organ Donation," *Critical Care Medicine* 38, no. 3 (2010): 963-70.

5. "Deceased Donors Recovered in the U.S. by Circumstance of Death, National Data: January 1, 1988-December 31, 2023," U.S. Department of Health and Human Services, Health Resources and Service Administration, Organ Procurement and Transplantation Network, at https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/#. To reach the results reported in our text, first, choose the category "Donor" and choose "All Organs." Then, choose this report: *All Donors by Donor Type*. After the screen changes, select "Add field to report: Donation after Circulatory Death (DCD)." The results displayed for 2023 were 10,442 in what the OPTN terms the "Brain Death Donor" category and 5894 in the "DCD Donor" category.

6. L. Jing et al., "Organ Preservation: From the Past to the Future," *Acta Pharmacologica Sinica* 39, no. 5 (2018): 845-57.

7. B. Domínguez-Gil et al., "Expanding Controlled Donation after the Circulatory Determination of Death: Statement from an International Collaborative," *Intensive Care Medicine* 47, no. 3 (2021): 265-81.

8. A. S. Shah, "Normothermic Regional Perfusion in Donor Heart Recovery: Establishing a New Normal," *Journal of Thoracic and Cardiovascular Surgery* 164, no. 1 (2022): 142-46; J. Couzin-Frankel, "Giving Heart," *Science* 380 (2023): 572-76.

9. L. B. Johnson et al., "Successful Emergency Transplantation of a Liver Allograft from a Donor Maintained on Extracorporeal Membrane Oxygenation," *Transplantation* 63, no. 6 (1997): 910-11; G. C. Oniscu et al., "In Situ Normothermic Regional Perfusion for Controlled Donation after Circulatory Death—the United Kingdom Experience," *American Journal of Transplantation* 14 (2014): 2846-54; C. Fondevila et al., "Liver Transplant Using Donors after Unexpected Cardiac Death: Novel Preservation Protocol and Acceptance Criteria," *American Journal of Transplantation* 9, no. 7 (2007): 1849-55.

10. American College of Physicians, "Ethics, Determination of Death, and Organ Transplantation in Normothermic Regional Perfusion (NRP) with Controlled Donation after Circulatory Determination of Death (cDCD): American College of Physicians Statement of Concern," April 17, 2021, https://www.acponline.org/sites/default/files/documents/clinical_information/resources/end_of_life_care/ethics_determination_of_death_and_organ_transplantation_in_nrp_2021.pdf, p. 4.

11. M. DeCamp, L. S. Sulmasy, and J. J. Fins, "POINT: Does Normothermic Regional Perfusion Violate the Ethical Principles Underlying Organ Procurement? Yes," *Chest* 162, no. 2 (2022): 288-90; A. K. Glazier and A. M. Capron, "Normothermic Regional Perfusion and US Legal Standards for Determining Death Are Not Aligned," *American Journal of Transplantation* 22 (2022): 1289-90; H. Peled et al., "Normothermic Regional Perfusion Requires Careful Ethical Analysis before Adoption into Donation after Circulatory Determination of Death," *Critical Care Medicine* 50 (2022): 1644-48.

12. E. Alamouti-fard et al., "Normothermic Regional Perfusion Is an Emerging Cost-Effective Alternative in Donation after Circulatory Death (DCD) in Heart Transplantation," *Cureus* 14, no. 6 (2022) doi:10.7759/cureus.26437; B. Parent et al., "Ethical and Logistical Concerns for Establishing NRP-cDCD Heart Transplantation in the United States," *American Journal of Transplantation* 20, no. 6 (2020): 1508-12; J. Basmaji et al., "Paving the Road for the Adoption of Normothermic Regional Perfusion in Canada," *Critical Care Explorations* 3, no. 11 (2021): doi:10.1097/CCE.0000000000000553.

13. B. L. Adams et al., "cDCDD-NRP Is Consistent with US Legal Standards for Determining Death," *American Journal of Transplantation* 22, no. 10 (2022): 2302-5; A. E. Wall et al., "Applying the Ethical Framework for Donation after Circulatory Death to Thoracic Normothermic Regional Perfusion Procedures," *American Journal of Transplantation* 22, no. 5 (2022): 1311-15; B. Parent et al., "Response to American College of Physician's Statement on the Ethics of Transplant after Normothermic Regional Perfusion," *American Journal of Transplantation* 22, no. 5 (2022): 1307-10.

14. A. Manara et al., "Maintaining the Permanence Principle for Death during In Situ Normothermic Regional Perfusion for Donation after Circulatory Death Organ Recovery: A United Kingdom and Canadian Proposal," *American Journal of Transplantation* 20, no. 8 (2020): 2017-25.

15. R. Choi, M. Tuppeny, and A. Reynolds, "The Ethical Conundrums of Normothermic Regional Perfusion," *Currents*, June 14, 2023, https://currents.neurocriticalcare.org/Leading-Insights/Article/the-ethical-conundrums-of-normothermic-regional-perfusion; S. Hughes, "Does New Heart Transplant Method Challenge Definition of Death?," *Medscape*, March 23, 2023, https://www.medscape.com/viewarticle/989937; J. L. Bernat et al., "Understanding the Brain-Based Determination of Death When Organ Recovery Is Performed with DCDD In Situ Normothermic Regional Perfusion," *Transplantation* 107, no. 8 (2023): 1650-54.

16. A. E. Wall et al., "The American Society of Transplant Surgeons Consensus Statement on Normothermic Regional Perfusion," *Transplantation* 108, no. 2 (2024): 312-18, at 316.

17. Ibid., 317.

18. Ibid., 317.

19. President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *Defining Death: Medical, Legal and Ethical Issues in the Determination of Death* (Washington, D.C.: U.S. Government Printing Office, 1981), 2.

20. H. C. M. A. Black, ed., *Black's Law Dictionary*, 4th ed. (St. Paul, MN: West Publishing Company, 1968), 488.

21. "Guidelines for the Determination of Death: Report of the Medical Consultants on the Diagnosis of Death to the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research," *Journal of the American Medical Association* 246 (1981): 2184-86, at 2185. The report was also included as appendix F, "Guidelines for the Determination of Death" (pp. 159-66), in the President's Commission's *Defining Death*.

22. Bernat et al., "The Circulatory-Respiratory Determination of Death in Organ Donation"; J. L. Bernat, "How the Distinction between 'Irreversible' and 'Permanent' Illuminates Circulatory-Respiratory Death Determination," *Journal of Medicine and Philosophy* 35, no. 3 (2010): 242-55.

23. Basmaji et al., "Paving the Road for the Adoption of Normothermic Regional Perfusion in Canada."

24. Ibid.; Y. Joshi et al., "Donation after Circulatory Death: A New Frontier," *Current Cardiology Reports* 24, no. 12 (2022): 1973-81; DeCamp, Sulmasy, and Fins, "POINT," 288-89.

25. Adams et al., "cDCDD-NRP Is Consistent with US Legal Standards for Determining Death," 2303.

26. Wall et al., "Applying the Ethical Framework for Donation after Circulatory Death to Thoracic Normothermic Regional Perfusion Procedures," 1314.

27. Parent et al., "Response to American College of Physician's Statement," 1308.

28. Ibid., 1308.

29. Glazier and Capron, "Normothermic Regional Perfusion and US Legal Standards for Determining Death Are Not Aligned."

30. Adams et al., "cDCDD-NRP Is Consistent with US Legal Standards for Determining Death," 2303.

31. Basmaji et al., "Paving the Road for the Adoption of Normothermic Regional Perfusion in Canada," 2.

32. Adams et al., "cDCDD-NRP Is Consistent with US Legal Standards for Determining Death."

33. Ibid.

34. R. D. Truog, A. Flescher, and K. Ladin, "Normothermic Regional Perfusion—the Next Frontier in Organ Transplants?," *Journal of the American Medical Association* 329 (2023): 2123-24.

35. J. DuBois and E. Anderson, "Attitudes toward Death Criteria and Organ Donation among Healthcare Personnel and the General Public," *Progress in Transplantation* 16, no. 1 (2006): 65-73; I. Neiders and V. Dranseika, "Minds, Brains, and Hearts: An Empirical Study on Pluralism Concerning Death Determination," *Monash Bioethics Review* 38, no. 1 (2020): 35-48.

36. K. Zheng et al., "Public Understandings of the Definition and Determination of Death: A Scoping Review," *Transplantation Direct* 8, no. 5 (2022): doi:10.1097/TXD.0000000000001300; D. A. Shewmon, "Statement in Support of Revising the Uniform Determination of Death Act and in Opposition to a Proposed Revision," *Journal of Medicine and Philosophy* 48, no. 5 (2023), 453-77.

37. N. B. Murphy et al., "Rationale for Revisions to the Definition of Death and Criteria for Its Determination in Canada," *Canadian Journal of Anaesthesia* 70, no. 4 (2023): 558-69.

38. Bernat et al., "Understanding the Brain-Based Determination of Death When Organ Recovery Is Performed with DCDD In Situ Normothermic Regional Perfusion."

39. National Conference of Commissioners on Uniform State Laws, *Revised Uniform Anatomical Gift Act (2006) (Last Revised or Amended in 2009)* (Chicago: National Conference of Commissioners on Uniform State Laws, 2009).

40. B. Parent et al., "Regarding Normothermic Regional Perfusion: Arguing by Insistence Is Not a Strong Argument," *American Journal of Transplantation* 22, no. 6 (2022): 1729-30, at 1729.

41. Some proponents of not sharing information with surrogates about NRP surgical techniques claim that postmortem authorization for transplantation carries a less demanding standard for information sharing than that required for informed consent in cases involving a living patient. Assuming arguendo that a lower postmortem standard exists, since questions remain about whether donors whose circulation has been reestablished are dead, it would be prudent not to rely on a postmortem standard for information disclosure.

42. K. P. Croome et al., "American Society of Transplant Surgeons Recommendations on Best Practices in Donation after Circulatory Death Organ Procurement," *American Journal of Transplantation* 23, no. 2 (2023): 171-79, at 173.

43. This is sometimes referred to as "direct procurement and perfusion."

44. S. López-Martínez, C. Simón, and X. Santamaria, "Normothermic Machine Perfusion Systems: Where Do We Go From Here?," *Transplantation* 108, no. 1 (2024): 22-44.

45. J. N. Schroder et al., "Expanding Heart Transplants from Donors after Circulatory Death (DCD)—Results of the First Randomized Controlled Trial Using the Organ Care System (OCS™) Heart—(OCS DCD Heart Trial)," *Journal of Heart and Lung Transplantation* 41, no. 4 (2022): S72; J. N. Schroder et al., "Transplantation Outcomes with Donor Hearts after Circulatory Death," *New England Journal of Medicine* 388, no. 23 (2023): 2121-31; N. K. Sweitzer, "Safely Increasing Heart Transplantation with Donation after Cardiac Death," *New England Journal of Medicine* 388, no. 23 (2023): 2191-92.

46. A. Page, S. Messer, and S. R. Large, "Heart Transplantation from Donation after Circulatory Determined Death," *Annals of Cardiothoracic Surgery* 7, no. 1 (2018): 75-81, at 75.

47. K. Mohkam et al., "In Situ Normothermic Regional Perfusion versus Ex Situ Normothermic Machine Perfusion in Liver Transplantation from

Donation after Circulatory Death," *Liver Transplantation* 28, no. 11 (2022): 1716-25.

48. S. P. Alexopoulos et al., "Adult Combined Heart-Liver Transplantation: The United States Experience," *Transplant International* 35 (2022): doi:10.3389/ti.2021.10036.

49. P. C. Groen, J. de Jonge, and R. J. Porte, "Prolonged Normothermic Machine Perfusion: Buying More Time for Liver Graft Assessment and Repair," *Transplantation* 107, no. 6 (2023): 1221-22.

50. D. Andrijevic et al., "Cellular Recovery after Prolonged Warm Ischaemia of the Whole Body," *Nature* 608 (2022): 405-12; M. Bona et al., "Cardiac Graft Assessment in the Era of Machine Perfusion: Current and Future Biomarkers," *Journal of the American Heart Association* 10, no. 4 (2021): doi:10.1161/JAHA.120.018966.

51. A. F. Sunjaya and A. P. Sunjaya, "Combating Donor Organ Shortage: Organ Care System Prolonging Organ Storage Time and Improving the Outcome of Heart Transplantations," *Cardiovascular Therapeutics* (2019): doi:10.1155/2019/9482797.

52. A. Page, S. Messer, and S. R. Large, "Heart Transplantation from Donation after Circulatory Determined Death," *Annals of Cardiothoracic Surgery* 7, no. 1 (2018): 75-81; D. Ghinolfi et al., "Sequential Use of Normothermic Regional and Ex Situ Machine Perfusion in Donation after Circulatory Death Liver Transplant," *Liver Transplantation* 27, no. 3 (2021): 385-402; J. E. Villanueva et al., "Expanding Donor Heart Utilization through Machine Perfusion Technologies," *Current Transplantation Reports* 9, no. 4 (2022): 219-26; J. Stehlik et al., "(620) First Report of the Transmedics Organ Care System Heart Perfusion Registry. A Multi-Institutional Outcomes Analysis," *Journal of Heart and Lung Transplantation* 42, no. 4 (2023): S277-78. We thank the anonymous reviewer who drew our attention to the point about NMP being a complementary, rather than solely a competing, technology.

53. D. O'Carroll, "What to Know about Heart Transplants," *Medical News Today*, August 31, 2022, https://www.medicalnewstoday.com/articles/heart-transplant-cost.

54. P. N. Martins and W. W. Williams, "To Cool or Not to Cool—Organ-Preservation Strategies in Transplantation," *New England Journal of Medicine* 388, no. 5 (2023): 468-69.

55. Bernat et al., "Understanding the Brain-Based Determination of Death When Organ Recovery Is Performed with DCDD In Situ Normothermic Regional Perfusion."

56. It seems unlikely that physicians' potential criminal or civil liability for performing NRP will be eliminated through a modification of the UDDA, since the committee appointed in 2021 by the Uniform Law Commission to revise that act was unable to reach a consensus on any points and suspended its work in September 2023. R. D. Truog and D. C. Magnus, "The Unsuccessful Effort to Revise the Uniform Determination of Death Act," *Journal of the American Medical Association* 330, no. 24 (2023): 2335-36.

57. OPTN Ethics Committee, "Ethical Analysis of Normothermic Regional Perfusion," UNOS Policy Department, 2023, https://optn.transplant.hrsa.gov/media/mq2m43uf/20240123-ethics_nrp_wp_final.pdf, p. 25.

58. Ibid., 25.

59. Ibid., 25.

60. Ibid., 25.

61. E. Sober, "Simplicity," in *A Companion to Epistemology*, ed. J. Dancy and E. Sosa (Malden, MA: Blackwell Publishers, 1992), 477-78, at 477.

62. J. A. Thomson et al., "Embryonic Stem Cell Lines Derived from Human Blastocysts," *Science* 282 (1998): 1145-47.

63. K. Takahashi et al., "Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors," *Cell* 131, no. 5 (2007): 861-72.

64. D. A. Robinton and G. Q. Daley, "The Promise of Induced Pluripotent Stem Cells in Research and Therapy," *Nature* 481 (2012): 295-305.

65. H. M. Blau and G. Q. Daley, "Stem Cells in the Treatment of Disease," *New England Journal of Medicine* 380 (2019): 1748-60; D. Goldenberg et al., "Regenerative Engineering: Current Applications and Future Perspectives," *Frontiers in Surgery* 8 (2021): doi:10.3389/fsurg.2021.731031.

66. J. W. Entwistle et al., "Normothermic Regional Perfusion: Ethical Issues in Thoracic Organ Donation," *Journal of Thoracic and Cardiovascular Surgery* 164, no. 1 (2022): 147-54, at 153.