

Reframing the Ethics of Normothermic Regional Perfusion

Normothermic Regional Perfusion (NRP) is a category of organ preservation techniques that have been used in procurement for controlled donation after circulatory-determined death (cDCD) for more than a decade. The general concept, after removing life-sustaining treatments and technologies from a donor patient and allowing for the appropriate stand-off period to declare death, involves regionally reperfusing vital organs inside the dead donor before procurement by applying extracorporeal membrane oxygenation (ECMO). Variations according to technique and organs procured notwithstanding, NRP shows promise for increasing organ availability in the United States, particularly for livers and hearts,¹ as has been the case in other countries.² While patient outcomes and organ viability are important for determinations of ethical appropriateness, the field is rapidly evolving; this work addresses ethical concerns given a medical or resource allocation advantage.

There are two commonly cited ethical concerns with NRP. First, reperfusing vital organs in situ raises concerns that this method of procurement violates the Dead Donor Rule (DDR) in that circulation of oxygenated blood, previously deemed irreversibly lost, is restored to a limited number of organs by region. Second, after death has been declared and before initiating ECMO, all NRP

techniques occlude potential blood flow to the brain – either singly or grouped with other organs. Some question whether this action, especially directly occluding flow to the brain only, intentionally hastens death or even creates a “brain death” situation. If even one of these concerns is validated, then NRP may be morally illicit.

This work explores both concerns by examining the actions of regional reperfusion in situ and occlusion of blood flow to the brain in the cDCD circumstance and demonstrates that NRP can be an ethical option for organ procurement; it also incorporates discussion of circumstances in the U.S. that have led to mistrust in organ procurement processes. This work relies on Entwistle’s comprehensive analysis and others for technical reference and offers additional considerations for Catholic health care.³

CIRCUMSTANCES

The clinical circumstances leading to cDCD are generally not equivocal. Although the patient does not meet the neurologic criteria to declare death (BD/DNC), medical and ethical standards indicate that withdrawing life sustaining treatment is appropriate, and this decision is separate and distinct from the decision to move forward with organ

procurement. In addition, the patient, or the patient's surrogate decision maker, has authorized and intends to donate organs. Once the decision has been made to withdraw life-sustaining treatments, the do not resuscitate order written, and medical interventions withdrawn, reinitiating life sustaining treatments would be medically and morally inappropriate.

DETERMINATION OF DEATH

In the United States, The Uniform Determination of Death Act (UDDA)⁴ stipulates that the determination of death must be made in accordance with accepted medical standards and provides two pathways for death to be determined: (1) irreversible cessation of circulatory and respiratory functions, or (2) irreversible cessation of all functions of the entire brain, including the brain stem. Debate regarding substituting the word permanent for irreversible notwithstanding, the conjunction "or" is key.

Neither pathway is prioritized over the other, and, although only one pathway must be satisfied, the whole person is dead. While much emphasis historically has been placed on the establishment of death by neurologic criteria as ethically sufficient for satisfying the DDR before organ procurement, it seems that today some ethicists prefer BD/DNC as being more morally legitimate than cDCD; but medical and legal standards say otherwise. If a person is declared dead by circulatory criteria, that person's brain is also dead by the same criteria because circulation to the whole body, including the brain, has ceased.^{5,6} The person is dead. This is one of the reasons that the term "brain death" is so unfortunate – because it gives

the impression that only the brain is dead when the person is dead by BD/DNC.

Within the Catholic tradition, Pope John Paul II condoned the concept of death determination by neurologic criteria, but he did not disavow death determination by cessation of circulatory and respiratory functions. Rather, he stated in the context of organ donation:

"With regard to the parameters used today for ascertaining death - whether the 'encephalic' signs or the more traditional cardio-respiratory signs - the Church does not make technical decisions... the criterion adopted in more recent times for ascertaining the fact of death, namely the complete and irreversible cessation of all brain activity, if rigorously applied, does not seem to conflict with the essential elements of a sound anthropology. Therefore a health worker professionally responsible for ascertaining death can use these criteria in each individual case as the basis for arriving at that degree of assurance in ethical judgement which moral teaching describes as 'moral certainty'".⁷

The notion that neurologic criteria of death must always be met to procure vital organs is inconsistent with the Holy See statement.

DOES OCCLUDING POTENTIAL BLOOD FLOW TO THE BRAIN AFTER A PATIENT DIES CHANGE THE KIND OF DEATH THAT HAS OCCURRED OR INTENTIONALLY CAUSE DEATH?

Some clinicians and at least one professional society⁸ have advanced the notion that occluding potential blood flow to the brain after death and before ECMO essentially

converts the circulatory-determined death to death by neurologic criteria. In addition to being illogical and unnecessary, this language is unhelpful for Catholics because it makes death the goal of an action and implies that the donor may not be dead yet. Dead people cannot die. As the Holy Father stated regarding determining death with certainty:

"...the death of the person is a single event, consisting in the total disintegration of that unitary and integrated whole that is the personal self. It results from the separation of the life-principle (or soul) from the corporal reality of the person. The death of the person, understood in this primary sense, is an event which no scientific technique or empirical method can identify directly."⁹

Medical standards change over time because the profession is constantly learning. Medical professionals rely on markers of death that have been demonstrated to be reliable, if not infallible, and imprecise language decreases confidence in those standards. A dead person cannot re-die; only a living person can die. And, if death is a single event, then one person should not be considered more dead than another person who has been declared dead by generally accepted medical, moral and legal standards.

Taken to its logical end, the concern for Catholics around this language is not that resuscitation is avoided, which is consistent with stated wishes, medical standards and the Catholic moral tradition. The concern, rather, is that this language provides reason to question whether the patient, in fact, might not be dead, and occluding flow to the brain would then be killing. Imprecise language, while not

necessarily indicative of truth, undermines confidence in medical standards and moral liceity of all cDCD. The whole notion smacks of conflicting interests and procurement slight-of-hand. Transparency, consistency and careful and precise language around the circumstances and process for declaring death is important.

WHY OCCLUDE FLOW TO THE BRAIN BEFORE APPLYING ECMO?

There are good reasons to occlude flow to the dead donor's brain before initiating ECMO, and they have to do with the kind of intervention ECMO is and the intentions and responsibilities of stakeholders. ECMO is generally considered a life-sustaining and even resuscitative intervention, but in NRP, ECMO is an organ preservation procedure. Circumstances matter; there is not – and should not be – any intention to resuscitate the dead donor. The intention of the medical team in occluding flow to the brain before initiating ECMO is to avoid resuscitating or even appearing to try to resuscitate the dead donor during organ preservation and testing. Procurement teams may express this in other ways, like stating that they are respecting the dead donor. It is the ethics community's job to sort through clinician's statements and meaning and offer guidance through ethical exploration and discourse.

The Permanence Principle has been utilized in countries where the definition of death following cessation of cardiorespiratory function is primarily based on brain perfusion (e.g., United Kingdom¹⁰), and it allows for reperfusion in situ of organs that will be procured using NRP as long as the brain is not reperfused.¹¹ This stipulation is logical

considering that death, so defined, has just been permitted to occur. The question is whether the same principle should apply in the U.S. or in Catholic health care, where the language defining the same reality of death is different.

Regarding circulatory death, Gardiner and colleagues note that, “The main justification for adopting permanent cessation over irreversible cessation... is that, in the great majority of cases, it is not ethically appropriate to attempt CPR or ECMO on such patients.”¹² This aligns with Bernat’s observation that “permanence is a perfect surrogate indicator for irreversibility” because spontaneous return of circulation will not happen and no intervention will be made to make it happen.¹³

The first and primary decision in the cDCD pathway is to withdraw treatments and technologies based on a wholistic assessment of clinical condition, standards, prognosis, treatment appropriateness and patient wishes. Although clinicians may have the technical ability to reverse the loss of cardiorespiratory function temporarily, it has already been determined that they do not have the ability to restore the patient’s health. Resuscitating a person from whom life-sustaining treatments have intentionally been withdrawn in these clinical circumstances is illogical, irresponsible and possibly illegal.

The debate has been ongoing for more than fifteen years in America. The American College of Physicians approves of using “permanent” in the cDCD domain but opposes in the BD/DNC domain.¹⁴ The American Academy of Neurology has transitioned to using the new verbiage in BD/DNC standards.¹⁵ The USCCB and NCBC strongly

stated opposition to substituting “permanent” for “irreversible” in brain death determinations, but they were less clear about their concerns in the cDCD realm, stating that this was a concern “during controlled circulatory death,” rather than using the word “after.”¹⁶ It is true that occluding flow to the brain during the stand-off period could be hastening death, but the same cannot be true after death has been declared unless the whole cDCD construct is illicit.

To be clear, this work only considers the use of the word “permanent” in the cDCD domain. If removing a heart after controlled circulatory-determined death for preservation outside of the donor’s body (direct procurement and perfusion) is not hastening death, then how could occluding blood vessels between the heart and brain have that result? These two actions have essentially the same effect on potential blood flow. The debate about verbiage is important and ongoing, but it should not distract from this issue; occluding blood vessels to the brain in a patient who is already dead does not hasten death.

DOES REGIONAL REPERFUSION IN SITU AFTER CIRCULATORY-DETERMINED DEATH RESTORE CIRCULATORY AND RESPIRATORY FUNCTION OF THE DEAD PERSON?

After death is determined by circulatory criteria, quickly reestablishing perfusion to the organs to be procured for transplantation optimizes future organ viability. NRP utilizes the dead donor’s body as the instrument of this activity by regions, and there are specific advantages to this methodology. In the United Kingdom,

where the Permanence Rule applies, re-establishing perfusion in the body but not in the brain conforms to ethical standards because of the way death is defined. How could the definition of circulatory-determined death in the U.S. be understood in a similarly useful way?

The word “function” warrants interpretive consideration. Is respiratory function (the natural purpose of the respiratory system¹⁷) to move air in and out of the body, or is it to oxygenate and ventilate blood? Similarly, is circulatory function to move blood through unintegrated portions of the body, or is the natural purpose of the circulatory system to perfuse the essential organs to be alive? Can there be circulatory function without perfusing the brain? The concept of regional perfusion is important because it does not allow for integrated function of the circulatory system; that is, at least one essential organ is not being perfused. ECMO can be used to perfuse and preserve organs by body region selectively. If the heart, lungs and brain are all reperfused together, ECMO could easily qualify as a (medically and ethically inappropriate) resuscitative measure, but circulatory function is not achieved without the brain.

Another practical consideration is whether perfusing the brain would serve to meet any transplant objectives. The brain is not

transplantable and will not be procured, so there is no reason to perfuse it. So, given the medical circumstances of the decision to withdraw life-sustaining treatments, the morally and legally valid declaration of death, the intentions of the patient to donate organs and the transplant team to preserve organs and not resuscitate the patient, and the absence of any future use of the brain in transplantation, there should be no moral issue with occluding flow to the brain and then initiating ECMO for organ preservation in the dead donor’s body.

The concept of regional perfusion begs further analysis. The difference in perfusing the brain and the legs, for example, is that the legs do not contain vital organs, and the legs do not define death. Because the legs do not contain vital organs perfusion is not necessary to achieve the medical goals, and since they are not involved in defining death, there is greater latitude in perfusion decisions. Clinical circumstances and professional judgment determine whether to perfuse them. While techniques vary by procurement goals, donor condition, clinician training, and resources, procurement teams approach regional perfusion decisions with intention.¹⁸ They are not applying ECMO in a manner consistent with a resuscitation of a person. See Table 1 for additional, though not comprehensive, considerations about regional perfusion.

TABLE 1: REGIONAL PERFUSION CONSIDERATIONS FOR NRP

| Region | Vital Organs | Defines Death | Transplantable Vital Organs | Regional Perfusion Details | Perfusion Benefit | Recommendation |
|-------------------|--------------|---------------|-----------------------------|--|-------------------|--|
| Head | Y | Y | N | Avoids donor resuscitation. Always excluded. Procedure near cannulation site prior to ECMO in TA NRP | N | Do not perfuse |
| Upper Extremities | N | N | N | If perfused, could result in collateral circulation to brain | N | Do not perfuse |
| Thorax | Y | Y | Y | Occluded for abdominal only NRP: <ul style="list-style-type: none"> • also occludes head/UE • additional procedure on thoracic aorta | Y | Perfuse for heart and/or lung procurement |
| Abdomen | Y | N | Y | Not occluded: <ul style="list-style-type: none"> • location of most vital organs • chemical advantage | Y | Perfuse per procurement goals and clinical circumstances |

MOVING FORWARD IN CATHOLIC HEALTH CARE

Decisions to adopt clinical practices and technologies are not made in a vacuum. That is, Catholic moral reasoning is applied within the U.S. construct of health care policy and medical standards. In recent years, trust in organ procurement has deteriorated largely due to system-based challenges. It is important that Catholic hospitals recognize these challenges and engage with Organ Procurement Organizations (OPO) and policy makers to improve relationships and align work toward optimizing organ availability and resources to serve humanity.

Recent Center for Medicare and Medicaid Services (CMS) OPO certification changes have created pressure on OPOs that has led to more aggressive enforcement of first-person authorization and forced hospitals to take sides.¹⁹ While the U.S. purports having an opt-in system, first-person authorization may be interpreted in ways that challenge whether the donor understands what their authorization means. First-person authorization has little in common with informed consent. Indicating a desire to be an organ donor in an advance medical directive, while somewhat more meaningful than checking a box while getting a driver's license, could be achieved with little or no conversation; families, who know and love the dying person, feel responsible. In these circumstances, the act of love that Catholics understand organ donation to be may even devolve into a legal battle. Considering that trust in health care is already low in America, this is not helpful.

Another issue, translation issues aside, is that different countries use different words to define

death. Many authors cited in this work urge international agreement in defining death, but agreement is difficult to reach across cultural, religious and legal boundaries. At a minimum, engaging and understanding circumstances, intentions and actions with precise language in communities of practice will promote trust and alignment.

Strategy and transparency are also important to promote trust. Changing too many variables at once is not helpful because correlations and causality become unclear. At present, it is best not to shorten the stand-off period to less than five minutes in NRP. In addition, identifying, owning and communicating areas of uncertainty to the broader medical community will improve alignment. There are additional issues related to facility resource utilization and clinical accountability that significantly affect organ procurement, and OPO agreements should be reviewed and adjusted, as needed and regularly.

Organ donation has always been received with suspicion because it attempts to achieve a moral good that exists at the boundaries of anthropological and religious values. Still, much has been achieved. NRP is one procurement category that evokes many valid questions for clinicians, religious leaders, ethicists and families, and these questions should be addressed systematically and transparently. For now, moving forward is possible if all parties agree on intentions, objectives, standards and moral constraints. ✚

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ENDNOTES

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