



**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**

Approved by the Board of Regents on April 17, 2021

The American College of Physicians (ACP) supports organ donation and transplantation and encourages all individuals to make their donation wishes known, especially to their loved ones but also through driver's license designation, advance directives, and conversations with their clinicians (1). Organs remain in short supply. A proposed method of organ retrieval, however, that uses what has been called normothermic regional perfusion (NRP) with controlled donation after circulatory determination of death (cDCD)--referred to as "NRP-cDCD"-- raises ethical questions and concerns.

Organ Donation

Organ donation occurs after circulatory determination of death (defined as death confirmed by the irreversible cessation of circulatory and respiratory functions) or after determination of brain death (defined as the irreversible loss of all brain functions, including the brain stem) (2).* Donation after determination of brain death (DBD) has been thought to result in higher quality organs for transplantation because the organs retrieved have been unaffected by loss of circulation and still exceeds donations after circulatory determination of death (DCD), but DCD has been increasing annually since 2007 (3). ACP supports both DCD and DBD when done transparently and in accordance with ethical and legal standards (1).

One way in which DCD proceeds is known as "controlled DCD," or cDCD, because it occurs after the planned withdrawal of life-sustaining therapies consistent with patient or family wishes. After withdrawal, when a patient's circulatory and respiratory functions cease, a "hands off" period of variable length (typically, 5 minutes) occurs (4). This is to confirm that the cessation of circulatory and respiratory functions is irreversible because there is no intention to resuscitate and auto-resuscitation is not possible. Death is then declared and rapid organ retrieval follows.

NRP-cDCD

While successful for many organs, cDCD has been rare for certain organs, such as the heart and intestines, which are more susceptible to the ischemic injury that occurs after irreversible cessation of circulation. As a result, there has been interest in developing ways to retrieve and reperfuse organs to minimize this injury. NRP-cDCD, performed in a few other countries, is being proposed for use in the United States (5,6). In NRP-cDCD, extracorporeal membrane

oxygenation (ECMO), cardiopulmonary bypass or other technologies are used after the “hands off” period to restore circulation to the vital organs or even to restart the heart (7). The aim is to preserve circulation to organs, thereby increasing the quality and number of organs for transplant. In addition, reperfusing *in situ* allows time to further assess organ function prior to explantation.

It is important to understand what NRP-cDCD entails. After determination of circulatory death, the donor’s chest is opened (as would normally happen in organ procurement). Recognizing the potential for restoration of circulation to result in *cerebral* reperfusion (either directly via the carotid or vertebral arteries, or indirectly via complex collateral circulations), various techniques such as ligating arteries or placing intravascular balloons or shunts are used to prevent cerebral reperfusion and bring on brain death (7). Perfusion is deemed regional, primarily because circulation to the brain has been actively excluded.

The donor is then quickly connected, via cannulation of large vessels, to an ECMO or bypass circuit that restores circulation and enables warm perfusion of the organs. This includes the heart, which may then resume beating. Thus, the determination of *irreversibility*--necessary for the certification of death of the patient made moments before--was apparently inaccurate since circulation is restored. And then, according to one protocol, “standard DBD procurement will commence” (6), because the patient is now dead by brain death criteria--due to actions taken by the physicians procuring the organs.

This protocol has been called “NRP-cDCD,” but this name lacks clarity and only describes part of what is going on. It is more accurately described as organ retrieval after cardiopulmonary arrest and the induction of brain death. The manner and declaration of death raise significant ethical questions and concerns.

Ethical Questions and Concerns

First, even though the goal of improving the number and quality of procured organs is an important one, here, the procedures and the operative definitions used to determine death seem orchestrated to serve that end. NRP-cDCD appears to violate one of the ethical foundations of organ donation, the “dead donor rule.” The dead donor rule specifies that donors cannot be made dead in order to obtain their organs and that organ retrieval cannot cause death (8,9). It promotes trust in organ transplantation and in medicine more generally by assuring patients, families, and the public that medicine will center on the individual patient’s best interests and not just the possible benefit to others, even if the need is great (10).

In NRP-cDCD, the patient is declared dead by the circulatory definition, which requires that cessation of circulatory and respiratory functions be irreversible (permanent). The intent, however, is to re-initiate circulation, and the patient is, in fact, successfully resuscitated. The question arises, does this violate the requirements for declaring death by circulatory criteria? Then, after declaring circulatory death, the cerebral circulation is deliberately occluded. This renders the patient brain dead so that circulation can be restored and the patient still be

considered dead, now by brain death, not circulatory death criteria (11). Death has not taken its natural course. Brain death has been caused in order to prevent brain reperfusion when circulation is restored. The purpose seems to be to justify reversing *what was supposed to be irreversible*: circulatory death.

Statements offered in support of NRP-cDCD should be scrutinized. For example, although some describe preventing cerebral circulation as ensuring “natural progression to complete cessation of brain function” (5), calling this a natural sequence is puzzling. NRP-cDCD requires a deliberate act intended to prevent the potential for recovery of brain function after reperfusion and the reversal of circulatory determination of death. The fact that mechanical failure of occlusive devices is possible, motivating proposals to include “safeguards” that monitor for and assure lack of cerebral perfusion (7), actually underscores the ethical significance of cerebral reperfusion (12).

Similarly, the possibility that reperfusion of the brain (were it not actively prevented) would be unlikely to restore consciousness or what some call “meaningful” neurologic function is not ethically relevant. Although the criteria for determining brain death vary internationally, the US definition of brain death requires the loss of all brain functions.

Even if the stated intent of NRP-cDCD is to preserve the organs (not to resuscitate the patient), this obscures and cannot be separated from what actually happens: NRP does resuscitate the patient. The assertion that NRP-cDCD is acceptable because the donor is in the process of dying lacks persuasiveness. The assertion that the donor has already been declared legally dead by another definition is also unpersuasive; because death had been declared does not mean that the declaration cannot be invalidated by subsequent acts. The ethical obligation to respect persons, including the dying and the dead, limit what can and should be done in organ retrieval. Is declaring a patient dead by irreversible circulatory criteria, then rendering the patient brain dead before restoring circulation honest, transparent and respectful of patient autonomy and dignity?

Second, ethical implications from the standpoint of justice must be examined. For example, even if DBD is still the most common method of donation, there are large numbers of drug overdose victims who have sustained irreversible and devastating hypoxic brain damage but who are not brain dead. In fact, DCD appears to be more common among overdose death donors when compared to other donors (e.g., trauma victims) (13). Calls to expand DCD following drug overdoses (14) could disproportionately affect an underserved and/or stigmatized population already burdened by the nation's substance abuse epidemic. Does this fulfill the requirements of justice for an equitable distribution of benefits and burdens within society?

Third, while as for all organ donations (1), proposed safeguards for NRP-cDCD are important, they alone cannot address more fundamental ethical problems. Ensuring that trained organ procurement facilitators separate from the donor's care team or the potential transplant

recipient's care team initiate discussion with a potential donor or donor's family is always critical, as is informed consent. If patients or family members of both the donor and recipient are not made aware of the full details of what this protocol involves, this lack of transparency can damage trust in health care and clinical research. More importantly, informed consent by itself cannot confer ethical legitimacy on NRP-cDCD: standards of medical ethics do not permit consent to supersede all other ethical considerations (just as patients should not receive medically contraindicated interventions on request, and research subjects should not be exposed to inappropriate risks even with their consent).

Fourth, *ex situ* alternatives to *in situ* NRP exist, including hypothermic and normothermic organ reperfusion that can be achieved by machines outside the body. Reperfusion devices can be applied after organs are procured via cDCD without restarting the donor's circulation or intentionally occluding brain perfusion (15) to render an individual brain dead. More research is needed on these devices. There is a large and ethically significant difference between perfusing an organ versus perfusing an individual.

Conclusion and Recommendation

It is tragic when a patient dies awaiting a needed organ. But organ procurement and transplantation must satisfy ethical standards in meeting this need. NRP-cDCD raises profound ethical questions regarding the dead donor rule, fundamental ethical obligations of respect, beneficence, and justice, and the categorical imperative to never use one individual merely as a means to serve the ends of another, no matter how noble or good those ends may be.

The questions and concerns raised here have not been adequately considered to date. Further professional and public discussion of NRP-cDCD— a protocol more accurately described as organ retrieval after cardiopulmonary arrest and the induction of brain death— is needed. ACP recommends the use of NRP-cDCD be paused. The burden of proof regarding the ethical and legal propriety of this practice has not been met. Sound ethical arguments, not just assertions, must underpin organ procurement methods and such efforts must be consistent with US legal and ethical standards for determination of death. Without this, we risk decreasing public confidence in health care and undermining support for organ donation, further exacerbating the problem this protocol seeks to address.

* We recognize that whether permanent is a better term than irreversible is a subject of debate. Irreversible, however, is the term standardly used in US law and medicine.

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