Donation after Cardiac Death in the US: History and Use

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When the clinical field of transplantation was in its infancy, cadaveric organs were recovered from donors declared deceased by cardiopulmonary criteria. Medical advances to sustain patients on life support, an increased understanding of the neurosciences, and guidelines to define death by the legal, scientific, and medical communities in the late 1960s and early 1970s produced a shift to the use of organs from brain dead donors. With the growing disparity between the number of donors and recipients, there is renewed interest in recovering organs from donors declared dead by cardiopulmonary criteria, known as donation after cardiac death (DCD). This review explores the historic nature of these shifts and describes them in the context of current organ use and outcomes.

Background

Since the introduction of cyclosporine in 1978, solid organ transplantation has become a highly successful modality for treating end-organ dysfunction, with enhanced quality of life, prolonged survival, or both. Such results created an increasing demand for transplantation, with a widening gap between the number of patients awaiting transplantation and available donors. According to the United Network of Organ Sharing, there are more than 88,000 patients waiting for an organ transplant in the US.¹ Approaches to an increased organ supply include expanding the use of living donors (kidney, liver, pancreas, small bowel, and lung), transecting an entire

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cadaveric organ into two transplantable portions (liver), and using organs from expanded criteria donors.²⁻⁸ DCD represents a small but increasing source of expanded criteria organs.⁹⁻¹⁴ Historically, DCD has been referred to as nonheart-beating donation (NHBD).

Currently in the US, the legal definition of death can be met by two different sets of criteria: cessation of cardiopulmonary function or cessation of whole brain function (Fig. 1). Since the mid 1970s, when brain death became legally accepted within the US, cadaveric organs have been obtained primarily from brain dead donors, who will also be referred to as deceased donors. Deceased donors are supported by mechanical ventilation and pharmacologic treatment. The next of kin provides consent for organ donation, and the donor is brought to the operating room for organ recovery. Organs from deceased donors are perfused by the donor's heart throughout the recovery process. Current estimates in the US indicate that 10,000 to 12,000 patients each year will meet the criteria for heart-beating organ donation.^{15,16}

In contrast to deceased donors, in the case of DCD, the donor must sustain loss of cardiopulmonary function to be declared dead, after which organ recovery can begin (Fig. 1). In the US, uncontrolled DCD is defined by the unexpected cessation of cardiopulmonary activity; in controlled DCD, cardiopulmonary arrest occurs after a planned withdrawal of care coordinated with organ recovery. DCD is additionally delineated by the European Maastricht classification (Fig. 2).17,18 Class 1 donors are defined as those who are dead on arrival to medical care; class 2 are those patients who arrive in extremis to medical care and have unsuccessful resuscitation; class 3 donors are those with terminal prognoses awaiting cardiac arrest; class 4 donors are brain dead patients who unexpectedly undergo cardiac arrest; and class 5 donors are inpatients who have documented cardiac arrest. Patients in classes 1, 2, 4, and 5 are considered uncontrolled donors and class 3 patients are controlled donors.

In the US, most DCDs are from controlled donors.

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Abbreviations and Acronyms

- DCD = donation after cardiac death
- ICP = intracranial pressure
- OPO = organ procurement organization IOM = Institute of Medicine

Generally, these are individuals with severe irreversible neurologic injury who do not meet the criteria of brain death or have other terminal conditions, such as a spinal fracture at the C2 vertebrae. The patient or next of kin has decided to withdraw care and has also given consent for organ donation. Organ donation may not take place until the patient undergoes cardiopulmonary arrest, and the donor is declared dead. Withdrawal of care is usually a planned event, typically taking place in the ICU or operating room. The surgical team is nearby and ready to recover the organs. From the time of extubation until recovery of the organs, the donor tissue undergoes warm ischemia. Anoxia, acidosis, loss of intracellular homeostasis, and activation of inflammatory pathways may occur during this period of time, characterizing the fundamental difference between deceased donation and DCD. Accumulating data suggest that despite the warm ischemia, in selected situations kidneys, livers, lungs, whole pancreata, and pancreatic islet cells obtained from these donors are functional and can be used in the transplant setting.19

Uncontrolled donors have an unexpected cessation of cardiopulmonary function. This could occur inside (ICU, emergency department) or outside the hospital setting. Lack of personnel for rapid recovery of organs, unknown lengths of hypotension, and organ hypoperfusion, prolonged periods of warm ischemia, and ethical and legal issues currently cloud the use of these donors in the US. To date, systems are being tested in Europe for the recovery and use of organs from uncontrolled donors.

Early transplantation outcomes with donation after cardiac death

Before 1968, cadaveric organ recovery was primarily through DCD. The great surgical strides of that decade demonstrated that abdominal and thoracic organs recovered from DCD could be successfully transplanted but were offset by poor longterm recipient survival (see proceeding text). At this time, the field of transplant immunology was in its early infancy and development of optimal preservation solutions was limited. Despite the science of transplantation lagging behind development of its surgical techniques, these early days served as the foundation for the future innovations to the field of solid organ transplantation (Table 1).

Kidney

The kidney was the first solid organ to be successfully transplanted in a human. In Boston in 1954, Dr Joseph Murray²⁰⁻²² transplanted a kidney from Ronald Herrick to Herrick's identical twin brother, Richard. In the spring of 1962, Dr Murray performed the first cadaveric transplant. Mel Doucette, a 23-year-old accountant received a renal graft from a 30-year old male donor who could not be separated from cardiopulmonary bypass after heart surgery.²³ The donor's body was maintained at 20° C on cardiopulmonary bypass while the recipient was brought to the operating room. The total ischemic time from death of the donor to revascularization in the recipient was 2 hours. The kidney began to function on the fifth postoperative day.

By the mid 1960s, several clinically active kidney transplantation programs existed, the largest at the University of Colorado under the direction of Dr Thomas Starzl. By 1967, registry data documented that recipients of cadaveric DCD organs had a 1-year survival of 23% to 38%; those with a living unrelated donor, 18% to 27%; and 1-year survival of 52% to 58% if the living donor was a sibling or parent.²⁴ It was recognized that prolonged ischemic time contributed to the poor results, with a 20% incidence of nonfunction.

Liver

Initial attempts at human liver transplantation in 1963 by Dr Starzl^{25,26} in Denver produced short-term survival. The first donor died of cardiac arrest on the operating room table during removal of a third ventricular brain tumor. Open cardiac massage was carried out for 45 minutes before death was declared, and extracorporeal perfusion was begun 15 minutes later. The recipient of this liver, Bennie Solis, a 3-year old boy with biliary atresia, ultimately succumbed to coagulopathic intraoperative hemorrhage.²⁷ The next two recipients died $7\frac{1}{2}$ and 22 days after transplantation, from pulmonary emboli.²⁷

In 1967, Starzl's group²⁸ reported the first series of liver transplantations with three of the initial seven patients alive at the time of the report, the longest surviving almost a year. The donors for these sets of transplanta-

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