ICU MANAGEMENT & PRACTICE

ICU Volume 13 - Issue 3 - Autumn 2013 - Matrix Features

Donation After Circulatory Determination of Death: A New Old Friend

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Organ transplantation has become a successful therapy for end-stage organ failure thanks to major advances in fields as essential as immunosuppression, transplant technology and intensive care.

Introduction

Although first transplants were carried out from asystolic donors, since the introduction of the brain-death concept

that followed the declaration of the Ad Hoc Committee of Harvard Medical School in the 1960s and the agreement of criteria for the diagnosis of brain death, heart-beating donors have become the main source of organs for transplantation. Despite many countries having reached maximum numbers of organ transplants, due to the efforts to optimise donation programmes in brain death, growing organ demand added to the epidemiological change in profile of the brain dead donor are leading to a feared situation of organ shortage and higher waiting lists.

Transplant teams have searched for alternative sources of organs for two decades. Living donation and reactivation of old programmes of donation after circulatory determination of death (DCDD) have contributed to mitigating this misfortune and expanding the donor pool.

Traditionally donors from a DCDD program have been considered as marginal donors because warm ischaemia time (WIT) following cardio-circulatory arrest (CCA) has important deleterious effects on organ viability. However, this problem has radically changed in recent years thanks to a better understanding of mechanisms involved in ischaemia- reperfusion injury. In this way, protective strategies against these insults that inevitably occur in these organs have been included in DCDD protocols. Actually long-term outcomes of DCDD are similar to brain-dead donation (BDD).

Terminology and Classification

DCDD is defined as donation that takes place after death has been confirmed by using circulatory criteria. Terminology applied to DCDD in the world has evolved over the years. Currently, we can find DCDD as other terms in the literature: non-heart-beating donation (NHBD) as opposed to heart-beating donation (HBD) or brain-dead donation (BDD), or donation after cardiac death (DCD). It is emphasised that the person's death is not determined by the irreversible loss of cardiac function, but by the irreversible loss of circulatory (and respiratory) function.

At the First International Workshop on NHBD held in Maastricht in 1995 four types of DCDD donors were clearly defined (Koostra et al. 1995):

I. Dead on arrival: patients who suffer a CCA are declared dead at an out-of-hospital site and brought to the hospital without any attempts of resuscitation.

II. Unsuccessful resuscitation: resuscitation attempts are made, but they are unsuccessful.

III. Awaiting cardiac arrest: patients with end-stage diseases such as irreversible brain damage, end-stage musculoskeletal disease, or severe spinal cord injury in whom withdrawal of life-sustaining therapy is considered and when it occurs, the subsequent CCA is awaited.

IV. Cardiac arrest in brain-dead patient: brain death is declared prior to an unanticipated CCA due to haemodynamic disturbances or the catecholamine storm during the brainstem herniation.

DCDD categories III and IV are classified as controlled DCDD (cDCDD), because CCA is always witnessed by a medical team and sometimes it can be expected and the transplant team can prepare for the procurement process. DCDD categories I and II are considered uncontrolled DCDD (uDCDD), because CCA is unexpected and the medical or transplant team is unaware of it.

Traditionally DCDD has been subdivided according to these Maastricht criteria, which are still widely used internationally. However, sometimes it is recognised that this classification is not accurate, and it does not reflect the DCDD reality held in clinical practice. In fact, DCDD has been classified in different ways by transplant teams, and the importance of discerning between CCA that takes place inside the hospital and outside it has been highlighted in uDCDD (Detry et al. 2012).

Donors can also be classified according to the phase of the donation process in which the person suffering the cessation of circulatory function remains. This classification has been recently published by the World Health Organization (WHO) within the Critical pathways for organ donation as part of an initiative to address the common challenges and make recommendations on how to maximise deceased donation (including BDD and DCCD) (Domínguez-Gil et al. 2011). The pathways provide clear definitions for potential, eligible, actual, and utilised donors, allowing better national and international comparisons to be made.

Warm Ischaemia Time

Knowledge of warm ischaemia time (WIT) as accurately as possible is critical to assess the viability of these organs for transplantation, because the ischaemia resulting from CCA induces a damage which may result in a reduced graft function in the recipient. In addition, there is large evidence that warm ischaemia exacerbates the deleterious effects of cold ischaemia.

In uDCDD WIT is defined as the time between witnessed circulatory arrest and the initiation of organ preservation manoeuvres. It is widely accepted that it should be less than 120-150 minutes and the time between CCA and initiation of cardiopulmonary resuscitation should be less than 15-30 minutes (Fondevila et al. 2007; Sánchez- Fructuoso et al. 2006) .

In cDCDD there is not worldwide consensus on the definition of WIT, but the interval of time between extubation (as the definitive withdrawal of treatment) until the initiation of preservation manoeuvres is the most commonly used (referred to as total WIT). But currently many of us prefer to register WIT as the time since the onset of a significant hypoperfusion (the first episode in which is recorded systolic blood pressure ≤ 60 or ≤ 50 mmHg determined by invasive arterial monitoring and/or oxygen saturation ≤ 80% determined by pulse oximetry) up to preservation manoeuvres (referred to as functional or true WIT) (Manara et al. 2012). Most transplant teams accept a maximum functional WIT of less than 60 minutes, although this time may be restricted to 30 minutes for a specific organ or donor.

Determination of Death

The determination of death is a critical phase in the process of donation, where professionalism, respect for fundamental ethical principles and transparency must be guaranteed. DCDD donors are declared dead using circulatory-respiratory criteria. Since the resumption of DCDD programmes an ongoing debate about the methods used for determination of both cessation of functions and its irreversibility has been established.

Cessation of circulatory functions is recognised by indirect measures of circulatory arrest (absence of heart sounds, pulse, blood pressure, respiratory effort). In a clinical setting of DCDD the use of confirmatory tests may be required in accordance with national or hospital protocols. Irreversibility is recognised by persistent cessation of function during an appropriate period of observation, but in the DCCD setting it is critical because it must be minimised to avoid an unnecessary increase of the WIT. This period, the so-called ‘no touch’ or ‘hands off’ period is stipulated as five minutes in Spain, but it can range from two to 20 minutes. This debate arises from the publication of some cases of autoresuscitation (spontaneous return of circulation) after failed attempts of CPR. A recent systematic review of autoresuscitation in DCDD donors showed no cases when invasive treatment was withdrawn (Bernat et al. 2010; Bernat et al. 2006).

Organ Preservation Techniques

In cDCDD, the most often used technique for preservation of abdominal organs consists of a laparotomy and cannulation of the aorta to start the cold flush, also called ‘super- rapid technique’. In uDCDD, chest compressions and ventilation are restored while the femoral vessels are cannulated after declaration of death in order to perform a normothermic regional perfusion (NrP), which involves maintaining blood temperature at 37ºC with a heat exchanger. An alternative technique is total body cooling, maintaining the blood temperature at 15ºC. Both systems have demonstrated the ability to reverse warm ischaemia injury, but the use of NrP changes the period of CCA (warm ischemia) into a period of preconditioning (ischaemic preconditioning) (Fondevila et al. 2007; Net et al. 2005). This technique reduces the incidence of delayed graft function compared to in situ perfusion.

After retrieval, organs must be preserved until the moment of the transplantation. Static cold storage (CS) has been traditionally used for all the organs. Nevertheless, various studies have focused their attention on organ preservation through the use of pulsatile perfusion machines (PM) until transplantation in the recipient. These studies have demonstrated an improvement in graft function in ischaemically damaged organs (Jochmans et al. 2011). This preservation technique reduces vascular resistances increased by the ischaemic insult and facilitates the elimination of erythrocyte residues from the microcirculation. PM is widely used in kidneys. Newly, an isolated liver PM has been developed, and it works in normothermia in order to add a period of normothermic recirculation ex vivo (Hessheimer et al. 2012).

Outcomes from DCDD

The outcomes are usually acceptable as long as the selection criteria of the DCDD donor are strict (age, NrP for a maximum of 240 minutes) The short- and mid-term outcomes of transplanted kidneys retrieved from DCDD donors are similar to those of kidneys retrieved from DBD donors (Wadei et al. 2013). In the case of livers, there is a higher incidence of primary graft failure and also a higher incidence of biliary duct complications (mainly intrahepatic ischaemic-type biliary strictures). Some of these recipients require retransplantation (Suárez et al. 2008). In the case of lungs, some studies have shown that the long-term patient and graft survival rates after DCDD donor lung transplantation are equivalent or better to those after BDD (de Antonio et al. 2007).

Conclusions

Worldwide implementation of DCDD programmes has mitigated the shortage of organs, with acceptable outcomes becoming an alternative to BDD. Further improvements in preservation techniques are needed to increase the organs for transplantation retrieved from potential DCDD donors.

For full references, please send a request to **editorial@icu-management.org**

Published on : Wed, 2 Oct 2013