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EDITORIAL

Multiorgan retrieval and preservation of the thoracic and abdominal organs in Maastricht III donors

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Abstract

This editorial describes the indications and technical aspects of the simultaneous retrieval of thoracic and abdominal organs in Maastricht III donors as well as the preservation of such organs until their implantation.

Key Words: Multiorgan retrieval; Abdominal organs; Thoracic organs; Maastricht III; Preservación; Transplantation

Core Tip: Every year approximately 100000 transplants are performed worldwide, which together with good success rates and the improvement of immunosuppressive medication means that indications for transplant are continually increasing. However, the imbalance between supply and demand of organs for transplantation means that the existing number of donors is insufficient for the large number of patients on waiting lists. Donation of organs after death needs to become an integral consideration as part of end-of-life care.

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INTRODUCTION

Organ transplantation is one of the most important advances in modern medicine, making it possible to increase the longevity and quality of life of transplant recipients, with patient and graft survival rates that were unimaginable just a few decades ago.

Every year approximately 100000 transplants are performed worldwide, which together with good success rates and the improvement of immunosuppressive medication means that indications for transplant are continually increasing. However, the imbalance between supply and demand of organs for transplantation means that the existing number of donors is insufficient for the large number of patients on waiting lists. Donation of organs after death needs to become an integral consideration as part of end-of-life care.

In Spain, due to efficient organization and public trust in the system and management of available resources, donation rates stand at 49 per million population (the highest in the world), although this supply still does not meet existing needs. There is, therefore, a need to further optimize the management of donation by tapping into new sources of organs. Currently, the most common type of donor for transplantation is the brain-dead donor, although in some centres, living donor transplantation programmes have been developed as an alternative, primarily for the kidney and liver.

Currently, we are witnessing renewed interest in organ procurement from donors after cardiocirculatory arrest. This type of donor was not previously accepted by most transplant teams due to the prolonged periods of ischaemia after cardiac arrest resulting in significant cell damage due to hypoxia. It should be remembered that before the brain death law was implemented in 1968, many organ donors were of this type, as it was necessary to wait for cardiocirculatory arrest to occur before harvesting organs.

In the 1980s transplant groups, especially in the United States and northern European countries, began including donation after cardiocirculatory arrest into their programmes. Kidneys were obtained either from living donors or from donors in asystole, who in English-language terminology have been called Non Heart Beating Donors, Donors after Cardiac Death or more recently and due to considerations related to the diagnosis of death Donors after the Circulatory Determination of Death (DCDD). Controlled Donation after Circulatory Determination of Death (cDCDD) is gradually becoming an important source of organs in countries with active programmes[1-4]. In Spain from 2010-2019, cDCDD accounted for up to 28% of total organ procurement activity[5].

In 1995, the first symposium on donation after cardiocirculatory arrest was held in Maastricht (The Netherlands), where three fundamental aspects were agreed upon: (1) Classification of donors after cardiac arrest (Non Heart Beating Donors) into four categories (Table 1); (2) Criteria for determining death after irreversible cardiac arrest; and (3) The period of time to wait between cardiac arrest and the start of organ harvesting.

In 1998, the United States Institute of Medicine published the consensus on transplantation with donors in irreversible cardiac arrest, recommending a non-touch time of 5 min, which became the standard time period for most groups[6]. However, a "no-touch period" attempts and varies widely between countries-protocols, ranging from 5 to 20 min[7].

Therefore, potential type III asystole donors are those patients with no apparent contraindications for donation who due to their admission pathology and subsequent evolution are expected to go into cardiorespiratory arrest after withdrawal of life-support measures within a period of time compatible with organ donation. The selection of donors is decided jointly with the family.

MAJORITY OF POTENTIAL MAASTRICHT TYPE III DONORS

The majority of potential Maastricht type III donors are patients with severe neurological pathology with a catastrophic functional prognosis and in whom progression to brain death is not foreseeable. Other patients may come from respiratory and/or cardiological medical pathologies with unfavourable evolution and prognosis, in whom the therapeutic measures applied have proved ineffective. There is no absolute age limit for controlled asystole donation, but it tends to be more restrictive than for brain death donation. In general, it depends on the organ to be transplanted, but a limit of 65-70 years has been established, although this limit is likely to be re-evaluated as experience is gained with this type of donation.

Current protocol recommendations are that the time elapsed between extubation and cardiorespiratory arrest should not exceed 2 h, although this time is debatable, as the haemodynamic and respiratory conditions of the patient after extubation are potentially more important.

The medical criteria for organ selection do not differ from the general criteria for brain death donation, although they are usually more restrictive. With regard to family consent, specific consent must be obtained for femoral vessel cannulation, heparin administration as well as administration of organ preservation drugs prior to death. Once mechanical ventilation has been withdrawn, periods of hypotension, hypoxia or anuria should be recorded. Sedation should be administered as necessary to ensure the patient's comfort and well-being, in accordance with recommendations on the management

Table 1 Donors after Cardiac Death Maastricht classification

Category	Type	Circumstances
1	Uncontrolled	Dead on arrival
2	Uncontrolled	Unsuccessful resuscitation
3	Controlled	Cardiac arrest follows planned withdrawal of life sustaining treatments
4	Either	Cardiac arrest in a patient who is brain dead

of the critically ill patient at the end of life from the relevant bioethics committee.

The death of the patient will be confirmed by a doctor responsible for the Critical Care Unit where the patient is admitted and who is not involved in the donation process, after confirming the absence of a curve in the arterial monitoring, the absence of breathing and the absence of response to stimuli for a period of 5 min. International recommendations on the type III donation procedure have recently been published that help define and clarify the most debated aspects of this type of donation[8].

In many hospitals, the multiorgan harvesting of abdominal organs in cDCDD is performed using a rapid harvesting technique. However, in recent years, the procurement of organs from asystole has developed significantly in Spain. Several centres are now pioneering the use of abdominal normothermic regional perfusion (NRP) with extracorporeal membrane oxygenation (ECMO) devices as a strategy for in situ blood reperfusion in both controlled and uncontrolled Donors after Cardiac Death [9-11]. Simultaneous thoracic and abdominal organ harvesting in controlled asystole type III donors is based on normothermic ECMO technology. NRP has the potential to decrease or ameliorate ischaemic injury and facilitate the testing of graft viability, reducing the percentage of organs discarded before transplantation.

One of the important advantages of the Spanish system is that it is legally authorised to initiate anticoagulation manoeuvres and placement of cannulae with consent.

Functional warm ischaemia time for abdominal grafts is defined as the time from systolic blood pressure < 60 mmHg to the onset of NRP (5 min of non-contact period included). For functional warm ischaemia time, an upper time limit of 30 min is set for the liver, pancreas and heart and 60 min for lungs and kidneys. In the intensive care unit, heparin administration (300-500 units/kg) and cannulation of the femoral vessels is performed prior to withdrawal of life support therapies. The femoral artery and femoral vein are cannulated, and an aortic balloon occlusion is placed in the contralateral groin to prevent cerebral and coronary perfusion during NRP. The goal of performing abdominal NRP is to maintain a pump flow of 2.0-2.4 L/min. A continuous pressure of 60-65 mmHg and a temperature of 37 °C should be maintained at the femoral arterial cannula; bicarbonate is administered after NRP is initiated to maintain a pH of 7.35-7.45, and a haematocrit > 25% is targeted.

Whilst NRP appears to be the ideal method for abdominal grafts, the lungs are removed from the donor in controlled asystole using the rapid extraction technique, by lowering the lung temperature with topical cooling as quickly as possible. This combined method was first described in the United Kingdom[12]. Our group has proposed a variant of the technique with premortem interventions, in which the risk of possible trans-diaphragmatic cooling of the liver is minimized[13]. However, there is still some reluctance among practitioners to combine the lung cooling and rapid retrieval technique with NRP for abdominal grafts. This method increases the complexity of the procurement procedure and might injure the grafts due to double temperature (low temperature affecting the liver and normothermia affecting the lungs) or due to inadequate perfusion pressure in the pump as a result of bleeding in the thorax after removal of the cardiopulmonary block or after vena cava clamping. From a technical point of view, once death is determined and NRP is initiated, a rapid sternotomy is performed. At the same time, the donor is reintubated and ventilated 5 min after NRP with 100% oxygen and a positive end-expiratory pressure of 5 cm H2O. The pulmonary artery is cannulated for cold lavage perfusion with Perfadex® (50 mL/kg). One litre of saline at 4 °C is administered in both hemithoraces for topical cooling, and the superior vena cava is ligated to separate the thoracic and abdominal compartments. Once the lungs are preserved with Perfadex® solution, lung extraction is performed using the same technique as for Donors after Cardiac Death donors.

To avoid low blood flow in the pump due to the absence of venous return from the thorax and head, 1.0-1.5 L of saline are administered to the cDCDD donor just before ligation of the vena cava. After perfusing the pulmonary artery with preservation solution, a laparotomy is performed to assess the appearance of the abdominal grafts by placing a cannula in the inferior mesenteric vein. After 2 h of NRP, the ECMO device is stopped, and a rapid dual cold organ perfusion is performed.

The retrieval of the kidneys, pancreas and liver is performed in the conventional way with the same surgical technique used in brain death donation, as haemodynamic stabilisation due to perfusion with NRP allows a completely controlled sequence of dissection and extraction. Perfusion with preservation solutions allows the kidneys, pancreas and liver to be obtained in optimal conditions for implantation.

Blood samples are taken from the ECMO device immediately after starting the NRP and at least every 30 min. Biochemistry, serum lactate levels and haematocrit are analysed. If alanine transaminase or aspartate transaminase exceed four times the upper limit of normal during NRP, the liver and pancreas are ruled out, even with a normal macroscopic appearance. Lactate levels are also monitored during NRP.

Ethical questions have been raised about the use of abdominal NRP and premortem interventions in cDCDD such as the possibility of restoring cerebral circulation after declaration of death if the aortic balloon occlusion technique fails. A specific methodology to avoid restoration of cerebral circulation after determination of death when using NRP and antemortem cannulation has recently been described and validated in a multicentre study[14]. This approach avoids the aforementioned ethical concern by guaranteeing the absence of cerebral resuscitation.

In the last 5 years the use of thoraco-abdominal NRP (TA-NRP) has made heart transplantation feasible and allows practitioners to assess heart function before organ procurement without any negative impact on the preservation of abdominal organs. The combined retrieval of lungs, heart and abdominal grafts using TA-NRP has been performed successfully in our centre. The use of TA-NRP in cDCDD heart donors in conjunction with cold storage following retrieval can eliminate the need to use *ex situ* machine perfusion devices, making cDCDD heart transplantation economically possible in other countries[15-17].

CONCLUSION

In summary, the use of TA-NRP for heart, lung and abdominal grafts or the combined approach (rapid recovery of the lungs and NRP for abdominal grafts) offers a remarkable recovery rate and is safe for thoracic organs (heart and lungs). Furthermore, abdominal grafts can benefit from the use of NRP as a preservation procedure. As this is a promising initial experience, further studies are needed to confirm our findings in the combined thoracic and abdominal procurement procedure.

FOOTNOTES

Author contributions: Casanova D designed the research, analysed the data and wrote the paper; Castillo F performed the research and analysed the data; Miñambres E performed the research and analysed the data; All authors wrote, read and approved the final manuscript.

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